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(54) **STABILIZED FORMULATIONS CONTAINING ANTI-ANG2 ANTIBODIES**(71) Applicants: **Scott M. Walsh**, Tarrytown, NY (US); **Daniel B. Dix**, LaGrangeville, NY (US)(72) Inventors: **Scott M. Walsh**, Tarrytown, NY (US); **Daniel B. Dix**, LaGrangeville, NY (US)(73) Assignee: **Regeneron Pharmaceuticals, Inc.**, Tarrytown, NY (US)

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(58) **Field of Classification Search**

None

See application file for complete search history.

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Primary Examiner — Brian J Gangle*Assistant Examiner* — Andrea McCollum(74) *Attorney, Agent, or Firm* — Alston & Bird LLP; Aparna G. Patankar(57) **ABSTRACT**

The present invention provides pharmaceutical formulations comprising an antibody that specifically binds to angiopoietin 2 (Ang-2). The formulations may contain, in addition to an anti-Ang-2 antibody, at least one amino acid, at least one sugar, or at least one non-ionic surfactant. The pharmaceutical formulations of the present invention exhibit a substantial degree of antibody stability after storage for several months and after being subjected to thermal and other physical stress.

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**STABILIZED FORMULATIONS CONTAINING
ANTI-ANG2 ANTIBODIES**
PARENT CASE TEXT

This application claims priority to U.S. Provisional Patent Application No. 61/589,427 filed on Jan. 23, 2012, the contents of which are incorporated herein by reference in their entirety.

SEQUENCE LISTING

An ST.25 compliant computer readable text file of a sequence listing is filed concurrently with the present specification according to PCT Rule 5.2 and Administrative Instructions Section 802. The contents of the text file are herein incorporated by reference. A paper copy of the sequence listing, which is identical in content to the ST.25 compliant computer readable text file, is included as part of the present specification and is herein incorporated by reference.

FIELD

The present invention relates to the field of therapeutic antibody formulations. More specifically, the present invention relates to the field of pharmaceutical formulations comprising an antibody that specifically binds to angiopoietin-2 (Ang-2).

BACKGROUND

Angiogenesis is the biological process whereby new blood vessels are formed. Aberrant angiogenesis is associated with several disease conditions including, e.g., proliferative retinopathies, rheumatoid arthritis, and psoriasis. In addition, it is well established that angiogenesis is critical for tumor growth and maintenance. Angiopoietin-2 (Ang-2) is a ligand for the Tie-2 receptor (Tie-2) and has been shown to play a role in angiogenesis. Ang-2 is also referred to in the art as Tie-2 ligand. (U.S. Pat. No. 5,643,755; Yancopoulos et al., 2000, Nature 407:242-248).

Antibodies and other peptide inhibitors that bind to Ang-2 are described to some extent in, e.g., U.S. Pat. Nos. 6,166,185; 7,521,053; 7,205,275; 2006/0018909 and 2006/0246071. There is a need in the art for novel Ang-2 modulating agents, including Ang-2 antibodies, that can be used to treat diseases and conditions caused by or exacerbated by angiogenesis.

Therapeutic antibodies must be formulated in a manner that not only makes the antibodies suitable for administration to patients, but also in a manner that maintains their stability during storage and subsequent use. For example, therapeutic antibodies in liquid solution are prone to degradation, aggregation, or undesired chemical modifications unless the solution is formulated properly. The stability of an antibody in liquid formulation depends not only on the kinds of excipients used in the formulation, but also on the amounts and proportions of the excipients relative to one another. Furthermore, other considerations aside from stability must be taken into account when preparing a liquid antibody formulation. Examples of such additional considerations include the viscosity of the solution and the concentration of antibody that can be accommodated by a given formulation, and the visual quality or appeal of the formulation. Thus, when formulating a therapeutic antibody, great care must be taken to arrive at a formulation that remains stable, contains an adequate con-

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centration of antibody, and possesses a suitable viscosity as well as other properties which enable the formulation to be conveniently administered to patients.

Antibodies to the angiopoietin-2 protein (Ang-2) are one example of a therapeutically relevant macromolecule that requires proper formulation. Although some anti-Ang-2 antibodies are known, there nonetheless remains a need in the art for novel pharmaceutical formulations comprising anti-Ang-2 antibodies that are sufficiently stable and suitable for administration to patients.

SUMMARY

The present invention satisfies the aforementioned need by providing pharmaceutical formulations comprising a human antibody that specifically binds to human angiopoietin-2 (Ang-2)

In one aspect, a liquid pharmaceutical formulation is provided, comprising: (i) an antibody that specifically binds to angiopoietin-2 (Ang-2); (ii) a buffer; (iii) an organic cosolvent; and (iv) a stabilizer.

In one embodiment, the antibody is provided at a concentration from about 5 ± 0.75 mg/mL to about 150 ± 22.5 mg/mL. In another embodiment, the antibody is provided at a concentration of about $5\text{ mg/mL}\pm0.75$ mg/mL. In another embodiment, the antibody is provided at a concentration of about $25\text{ mg/mL}\pm3.75$ mg/mL. In another embodiment, the antibody is provided at a concentration of about $50\text{ mg/mL}\pm7.5$ mg/mL.

In some embodiments, exemplary anti-Ang-2 antibodies and Ang-2 antigen-binding fragments of the invention comprise HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 domains, respectively, selected from the group consisting of: (i) SEQ ID NO: 4, 6, 8, 12, 14 and 16 (e.g., H1H685); (ii) SEQ ID NO: 28, 30, 32, 36, 38 and 40 (e.g., H1H690); (iii) SEQ ID NO: 52, 54, 56, 60, 62 and 64 (e.g., H1H691); (iv) SEQ ID NO: 148, 150, 152, 156, 158 and 160 (e.g., H1H696); (v) SEQ ID NO: 196, 198, 200, 204, 206 and 208 (e.g., H1H706); (vi) SEQ ID NO: 268, 270, 272, 276, 278 and 280 (e.g., H1M724); and (vii) SEQ ID NO: 436, 438, 440, 444, 446 and 448 (e.g., H2M744).

In related embodiments, the invention comprises an anti-Ang-2 antibody or an antigen-binding fragment of an antibody which specifically binds Ang-2, wherein the antibody or antigen-binding fragment comprises the heavy and light chain CDR domains (i.e., CDR1, CDR2 and CDR3) contained within heavy and light chain variable domain sequences selected from the group consisting of SEQ ID NO: 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140, 142/144, 146/154, 162/164, 166/168, 170/178, 186/188, 190/192, 194/202, 210/212, 214/216, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 266/274, 282/284, 286/288, 290/298, 306/308, 310/312, 314/322, 330/332, 334/336, 338/346, 354/356, 358/360, 362/370, 378/380, 382/384, 386/394, 402/404, 406/408, 410/418, 426/428, 430/432, 434/442, 450/452, 454/456, 458/466, 474/476, 478/480, 482/490, 498/500, and 502/504. In one embodiment, the antibody or fragment thereof comprises the CDR sequences contained within HCVR and LCVR selected from the amino acid sequence pairs of SEQ ID NO: 18/20, 42/44, 66/68, 162/164, 210/212, 266/274, and 434/442.

In one embodiment, the pH of the liquid formulation is about pH 6.0 ± 0.5 , pH 6.0 ± 0.4 , pH 6.0 ± 0.3 , pH 6.0 ± 0.2 , pH 6.0 ± 0.1 , pH 6.0 ± 0.05 , pH 6.0 ± 0.01 , or pH 6.0. In a specific embodiment, the pH of the liquid formulation is about pH 6.0 ± 0.3 . In one embodiment, the liquid pharmaceutical buffer

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comprises one or more buffers, which has or have an effective buffering range of about pH 5.5 to about pH 7.4, or a pKa of about 6.0.

In one embodiment, the buffer is histidine. In one embodiment, the histidine is at a concentration of $5\text{ mM}\pm0.75\text{ mM}$ to $50\text{ mM}\pm7.5\text{ mM}$. In one embodiment, the histidine is at a concentration of $5\text{ mM}\pm0.75\text{ mM}$ or about 5 mM. In one embodiment, the histidine is at a concentration of $10\text{ mM}\pm1.5\text{ mM}$ or about 10 mM. In one embodiment, the histidine is at a concentration of $15\text{ mM}\pm2.25\text{ mM}$ or about 15 mM. In one embodiment, the histidine is at a concentration of $20\text{ mM}\pm3\text{ mM}$ or about 20 mM. In one embodiment, the histidine is at a concentration of $25\text{ mM}\pm3.75\text{ mM}$ or about 25 mM. In one embodiment, the histidine is at a concentration of $30\text{ mM}\pm4.5\text{ mM}$ or about 30 mM. In one embodiment, the histidine is at a concentration of $35\text{ mM}\pm5.25\text{ mM}$ or about 35 mM. In one embodiment, the histidine is at a concentration of $40\text{ nM}\pm6\text{ mM}$ or about 40 nM. In one embodiment, the histidine is at a concentration of $45\text{ mM}\pm6.75\text{ mM}$ or about 45 mM. In one embodiment, the histidine is at a concentration of $50\text{ mM}\pm7.5\text{ mM}$ or about 50 mM.

In one embodiment, the organic cosolvent is a nonionic polymer containing a polyoxyethylene moiety. In some embodiments, the organic cosolvent is any one or more of polysorbate 20, poloxamer 188 and polyethylene glycol 3350. In a specific embodiment, the organic cosolvent is polysorbate 20.

In one embodiment, the organic cosolvent is at a concentration of from about $0.005\%\pm0.000075\%$ to about $1\%\pm0.15\%$ "weight to volume" or "w/v", wherein, e.g., $0.1\text{ g/ml}=10\%$ and $0.01\text{ g/ml}=1\%$. In one embodiment, the organic cosolvent is polysorbate 20, which is at a concentration of about $0.2\%\pm0.03\%$ w/v. In another embodiment, the organic cosolvent is polysorbate 20, which is at a concentration of $0.01\%\pm0.0015\%$ w/v or about 0.01% w/v.

In one embodiment, the stabilizer is a sugar. In one embodiment, the sugar is selected from the group consisting of sucrose, mannitol and trehalose. In a specific embodiment, the stabilizer is sucrose.

In one embodiment, the stabilizer is at a concentration of from $1\%\pm0.15\%$ w/v to $20\%\pm3\%$ w/v. In a specific embodiment, the stabilizer is sucrose at a concentration of $5\%\pm0.75\%$ w/v or about 5% w/v. In another specific embodiment, the stabilizer is sucrose at a concentration of $7.5\%\pm1.125\%$ w/v or about 7.5% w/v. In another specific embodiment, the stabilizer is sucrose at a concentration of $10\%\pm1.5\%$ w/v or about 10% w/v. In another specific embodiment, the stabilizer is sucrose at a concentration of $12.5\%\pm1.875\%$ w/v or about 12.5% w/v. In another specific embodiment, the stabilizer is sucrose at a concentration of $15\%\pm2.25\%$ w/v or about 15% w/v. In another specific embodiment, the stabilizer is sucrose at a concentration of $20\%\pm3\%$ w/v or about 20% w/v.

In one embodiment, the viscosity of the formulation is about 1 cPoise to about 10 cPoise. In one embodiment, the viscosity of the formulation is $1.4\text{ cPoise}\pm0.21\text{ cPoise}$, or about 1.4 cPoise.

In one embodiment, the osmolality of the formulation is within a physiological range. In one embodiment, the formulation has an osmolality of about 300 milli-Osmoles per kilogram (mOsm) to about 400 mOsm. In one embodiment, the osmolality of the formulation is $363\text{ mOsm}\pm54\text{ mOsm}$, or about 363 mOsm.

In one embodiment, at least 96% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -80° C . is non-aggregated and un-degraded, as determined by size exclusion chromatogra-

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phy. In one embodiment, at least 55% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -80° C . is of the non-basic and non-acidic form (i.e., main peak or main charge form or "region 2 peak"), as determined by ion exchange chromatography.

In one embodiment, at least 96% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -30° C . is non-aggregated and un-degraded, as determined by size exclusion chromatography. In one embodiment, at least 55% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -30° C . is of the main charge form, as determined by ion exchange chromatography.

In one embodiment, at least 96% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -20° C . is non-aggregated and un-degraded, as determined by size exclusion chromatography. In one embodiment, at least 55% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after six months of storage at -20° C . is of the main charge form, as determined by ion exchange chromatography.

In one embodiment, at least 96% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after nine months of storage at 5° C . is of the non-aggregated and un-degraded form, as determined by size exclusion chromatography. In one embodiment, at least 56% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after nine months of storage at 5° C . is of the main charge form, as determined by ion exchange chromatography.

In one embodiment, at least 98% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after three months of storage at 25° C . is of the non-aggregated and un-degraded form, as determined by size exclusion chromatography. In one embodiment, at least 54% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after three months of storage at 25° C . is of the main charge form, as determined by ion exchange chromatography.

In one embodiment, at least 97% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after one month of storage at 37° C . is of the non-aggregated and un-degraded form, as determined by size exclusion chromatography. In one embodiment, at least 47% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after one month of storage at 37° C . is of the main charge form, as determined by ion exchange chromatography.

In one embodiment, at least 95% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after 28 days of storage at 45° C . is of the non-aggregated and un-degraded form, as determined by size exclusion chromatography. In one embodiment, at least 32% of the anti-Ang-2 antibody recovered from the liquid pharmaceutical formulation after 28 days of storage at 45° C . is of the main charge form, as determined by ion exchange chromatography.

In one aspect, a liquid pharmaceutical formulation is provided, comprising: (i) from $5\pm0.75\text{ mg/ml}$ to $150\pm22.5\text{ mg/ml}$ of a human antibody that specifically binds to human Ang-2; (ii) from $5\text{ mM}\pm0.75\text{ mM}$ to $50\text{ mM}\pm7.5\text{ mM}$ histidine; (iii) from $0.005\%\pm0.000075\%$ to $1\%\pm0.15\%$ (w/v) polysorbate 20; and (iv) from $1\%\pm0.15\%$ to $20\%\pm3\%$ (w/v) sucrose, at a pH of from about 5.5 to about 6.5. The anti-Ang-2 antibody of this aspect comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR) such that the HCVR/LCVR combination comprises heavy and light chain complementarity determining regions (HCDR1-HCDR2-HCDR3/LCDR1-LCDR2-LCDR3), which comprise the

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amino acid sequences of SEQ ID NOs:4-6-8/SEQ ID NOs: 12-14-16, respectively. In a particular embodiment, the anti-Ang-2 antibody comprises a heavy chain variable region (HCVR) and light chain variable region (LCVR) comprising an amino acid sequence of SEQ ID NO: 18 and SEQ ID NO: 20, respectively (antibody H1H685P of U.S. Pub. Pat. App. No. 20110027286, which is specifically incorporated herein by reference in its entirety).

In another embodiment, the liquid formulation comprises (i) 50 ± 7.5 mg/mL of H1H685P; (ii) 10 ± 1.5 mM histidine; (iii) $0.2\%\pm0.03\%$ (w/v) polysorbate 20; and (iv) $10\%\pm1.5\%$ (w/v) sucrose, at a pH of 6.0 ± 0.5 .

In one embodiment of this aspect, the liquid formulation comprises (i) 25 ± 3.75 mg/mL of H1H685P; (ii) 10 ± 1.5 mM histidine; (iii) $0.2\%\pm0.03\%$ (w/v) polysorbate 20; and (iv) $10\%\pm1.5\%$ (w/v) sucrose, at a pH of 6.0 ± 0.5 . In one embodiment of this particular formulation, after storage of the formulation at 45° for 28 days, $\geq95\%$ of the antibody is native and $\geq32\%$ of the antibody is of the main charge form. In one embodiment of this particular formulation, after storage of the formulation at 37° for one month, $\geq97\%$ of the antibody is native and $\geq47\%$ of the antibody is of the main charge form. In one embodiment of this particular formulation, after storage of the formulation at 25° for three months, $\geq98\%$ of the antibody is native and $\geq54\%$ of the antibody is of the main charge form. In one embodiment of this particular formulation, after storage of the formulation at 5° for nine months, $\geq96\%$ of the antibody is native and $\geq56\%$ of the antibody is of the main charge form. In one embodiment of this particular formulation, after storage of the formulation at -20° for three months, $\geq9\%$ of the antibody is native and $\geq55\%$ of the antibody is of the main charge form. In one embodiment of this particular formulation, after storage of the formulation at -80° for six months, $\geq96\%$ of the antibody is native and $\geq55\%$ of the antibody is of the main charge form.

In one aspect, a liquid pharmaceutical formulation of any of the preceding aspects is provided in a container. In one embodiment, the container is a polycarbonate vial. In another embodiment, the container is a glass vial. In one embodiment, the glass vial is a type 1 borosilicate glass vial with a fluorocarbon-coated butyl rubber stopper. In another embodiment, the container is a microinfuser. In another embodiment, the container is a syringe. In a specific embodiment, the syringe comprises a fluorocarbon-coated plunger. In one specific embodiment, the syringe is a 1 mL long glass syringe containing less than about 500 parts per billion of tungsten equipped with a 27-G needle, a fluorocarbon-coated butyl rubber stopper, and a latex-free, non-cytotoxic rubber tip cap. In a more specific embodiment, the syringe is a NUOVA OMPI 1 mL long glass syringe equipped with a 27-G thin wall needle, a FLUROTEC-coated 4023/50 rubber stopper, and a FM 27 rubber tip cap. In another specific embodiment, the syringe is a 1 mL or 3 mL plastic syringe fitted with a 27-G needle. In a more specific embodiment, the plastic syringe is distributed by BECTON DICKINSON. In one embodiment, the container is a polyvinyl chloride IV bag. In another embodiment, the container is a polyolefin IV bag.

In one aspect, a pharmaceutical formulation comprising (a) $50\text{ mg/mL}\pm7.5\text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10\text{ mM}\pm1.5\text{ mM}$ histidine, pH 6 ± 0.5 , (c) $0.2\%\text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\%\text{ w/v}\pm1.5\%$ sucrose is provided, wherein (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20, (b) over 96% of the antibodies in the formulation have a molecular weight of

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about $150.9\text{ kDa}\pm1\text{ kDa}$, (c) at least 53% of the antibodies in the formulation have an isoelectric point of about 8.13 ± 0.01 , (d) from about 90% to about 92% of the antibodies in the formulation are fucosylated, and (e) about 2.5% of the heavy chains of the antibodies lack a C-terminal lysine.

In one embodiment, the pharmaceutical formulation consists of (a) $50\text{ mg/mL}\pm7.5\text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10\text{ mM}\pm1.5\text{ mM}$ histidine, pH 6 ± 0.5 , (c) $0.2\%\text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\%\text{ w/v}\pm1.5\%$ sucrose is provided, wherein (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20, (b) over 96% of the antibodies in the formulation have a molecular weight of about $150.9\text{ kDa}\pm1\text{ kDa}$, (c) at least 53% of the antibodies in the formulation have an isoelectric point of about 8.13 ± 0.01 , (d) from about 90% to about 92% of the antibodies in the formulation are fucosylated, and (e) about 2.5% of the heavy chains of the antibodies lack a C-terminal lysine.

In one aspect, a pharmaceutical formulation comprising (a) $25\text{ mg/mL}\pm3.75\text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10\text{ mM}\pm1.5\text{ mM}$ histidine, pH 6 ± 0.5 , (c) $0.2\%\text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\%\text{ w/v}\pm1.5\%$ sucrose is provided, wherein (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20, (b) over 96% of the antibodies in the formulation have a molecular weight of about $150.9\text{ kDa}\pm1\text{ kDa}$, (c) at least 53% of the antibodies in the formulation have an isoelectric point of about 8.13 ± 0.01 , (d) from about 90% to about 92% of the antibodies in the formulation are fucosylated, and (e) about 2.5% of the heavy chains of the antibodies lack a C-terminal lysine.

In one embodiment, the pharmaceutical formulation consists of (a) $25\text{ mg/mL}\pm3.75\text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10\text{ mM}\pm1.5\text{ mM}$ histidine, pH 6 ± 0.5 , (c) $0.2\%\text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\%\text{ w/v}\pm1.5\%$ sucrose is provided, wherein (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20, (b) over 96% of the antibodies in the formulation have a molecular weight of about $150.9\text{ kDa}\pm1\text{ kDa}$, (c) at least 53% of the antibodies in the formulation have an isoelectric point of about 8.13 ± 0.01 , (d) from about 90% to about 92% of the antibodies in the formulation are fucosylated, and (e) about 2.5% of the heavy chains of the antibodies lack a C-terminal lysine.

In one aspect, a kit comprising a pharmaceutical composition of any one of the preceding aspects, a container, and instructions is provided. In one embodiment, the container is a prefilled syringe. In one embodiment, the container is a borosilicate vial fitted with a FLUROTEC-coated 4023/50 rubber stopper.

Other embodiments of the present invention will become apparent from a review of the ensuing detailed description.

DETAILED DESCRIPTION

Before the present invention is described, it is to be understood that this invention is not limited to particular methods and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. As used herein, the term "about", when used in reference to a particular recited numerical value or range of values, means that the value may vary from the recited value

by no more than 2%. For example, as used herein, the expression “about 100” includes 98 and 102 and all values in between (e.g., 98.00, 98.01, 98.02, 98.03, 98.04, . . . , 101.96, 101.97, 101.98, 101.99, 102.00).

Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to describe in their entirety. Pharmaceutical Formulations

As used herein, the expression “pharmaceutical formulation” means a combination of at least one active ingredient (e.g., a small molecule, macromolecule, compound, etc. which is capable of exerting a biological effect in a human or non-human animal), and at least one inactive ingredient which, when combined with the active ingredient or one or more additional inactive ingredients, is suitable for therapeutic administration to a human or non-human animal. The term “formulation”, as used herein, means “pharmaceutical formulation” unless specifically indicated otherwise. The present invention provides pharmaceutical formulations comprising at least one therapeutic polypeptide. According to certain embodiments of the present invention, the therapeutic polypeptide is an antibody, or an antigen-binding fragment thereof, which binds specifically to human angiopoietin-2 (Ang-2) protein. More specifically, the present invention includes pharmaceutical formulations that comprise: (i) a human antibody that specifically binds to human Ang-2 (ii) a histidine buffer; (iii) an organic cosolvent that is a non-ionic surfactant; and (iv) a thermal stabilizer that is a carbohydrate. Specific exemplary components and formulations included within the present invention are described in detail below.

Antibodies that Bind Specifically to Ang-2

The pharmaceutical formulations of the present invention may comprise a human antibody, or an antigen-binding fragment thereof, that binds specifically to human Ang-2. As used herein, the term “Ang-2” or “ANG2” means a human angiopoietin-2, which is generally known as an autocrine antagonist of Tie2 activation. Ang-2 is generally known in the art to “prime” the vascular endothelium to receive the effects of cytokines. Ang-2 is strongly expressed in tumor vasculature, and is generally thought to act synergistically with other cytokines (i.e., vascular endothelial growth factor) to promote angiogenesis and tumor progression. An exemplary human Ang-2 amino acid sequence is described in SEQ ID NO: 518. Antibodies to human Ang-2 are described in patent application publications US 2010/0166768, US 2011/0065902, WO 2010/077854, and US 2011/0027286, which are herein incorporated by reference.

The term “antibody”, as used herein, is generally intended to refer to immunoglobulin molecules comprising four polypeptide chains: two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, as well as trimers thereof (e.g., IgM); however, immunoglobulin molecules consisting of only heavy chains (i.e., lacking light chains) are also encompassed within the definition of the term “antibody”. Each heavy chain comprises a heavy chain variable region (abbreviated herein as HCVR or V_H) and a heavy chain constant region. The heavy chain constant region comprises three domains, CH1, CH2 and CH3. Each light chain comprises a light chain variable region (abbreviated herein as LCVR or V_L) and a light chain constant region. The light chain constant region comprises one domain (CL1). The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementary determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L is composed

of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

Unless specifically indicated otherwise, the term “antibody”, as used herein, shall be understood to encompass complete antibody molecules as well as antigen-binding fragments thereof. The term “antigen-binding portion” or “antigen-binding fragment” of an antibody (or simply “antibody portion” or “antibody fragment”), as used herein, refers to 10 one or more fragments of an antibody that retain the ability to specifically bind to human Ang-2 or an epitope thereof.

An “isolated antibody”, as used herein, is intended to refer to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds human Ang-2 is substantially free of antibodies that specifically bind antigens other than human Ang-2).

The term “specifically binds”, or the like, means that an antibody or antigen-binding fragment thereof forms a complex with an antigen that is relatively stable under physiologic conditions. Specific binding can be characterized by a dissociation constant of at least about 1×10^{-6} M or greater. Methods for determining whether two molecules specifically bind are well known in the art and include, for example, equilibrium dialysis, surface plasmon resonance, and the like. An isolated antibody that specifically binds human Ang-2 may, however, have cross-reactivity to other antigens, such as Ang-2 molecules from other species (orthologs). In the context of the present invention, multispecific (e.g., bispecific) 20 antibodies that bind to human Ang-2 as well as one or more additional antigens are deemed to “specifically bind” human Ang-2. Moreover, an isolated antibody may be substantially free of other cellular material or chemicals.

Exemplary anti-human Ang-2 antibodies that may be 35 included in the pharmaceutical formulations of the present invention are set forth in patent application publications US 2010/0166768, US 2011/0065902, US 2011/0027286 and WO 2010/077854, the disclosures of which are incorporated herein by reference in their entirety.

According to certain embodiments of the present invention, the anti-human Ang-2 H1H685P antibody is a human IgG1 comprising a heavy chain variable region that is of the IGHV3-13.01 subtype and a light chain variable region that is of the IGKV3-20.01 subtype (see Barbie and Lefranc, The 40 Human Immunoglobulin Kappa Variable (IGKV) Genes and Joining (IGKJ) Segments, Exp. Clin. Immunogenet. 1998; 15:171-183; and Scaviner, D. et al., Protein Displays of the Human Immunoglobulin Heavy, Kappa and Lambda Variable and Joining Regions, Exp. Clin. Immunogenet., 1999; 16:234-240). The germline IGHV3-13 and IGKV3-20 sequences, and the amino acid position assignment numbers presented herein comport with the international Immunogenetics (IMGT) information system, as described in Lefranc, M.-P., et al., IMGT®, the international ImMunoGeneTics 45 information system®, Nucl. Acids Res, 37, D1006-D1012 (2009).

In some embodiments, the anti-human Ang-2 H1H685P comprises at least one amino acid substitution relative to the canonical heavy chain variable region, which results in a 50 change in the angle of rotation of the peptide chain within a CDR, which is reasonably expected to alter the exposed surface of the antibody relative to the germline IGHV3-13 sequence. In some embodiments, the amino acid substitution comprises the substitution of proline for the isoleucine at position 39 within CDR2 of IGHV3-13.

In some embodiments, the anti-human Ang-2 H1H685P antibody comprises at least one amino acid substitution,

which creates a charge change within the third CDR of the germline IGKV3-20. In some embodiments, the amino acid substitution or substitutions are selected from the group consisting of (a) a basic amino acid substituted for an uncharged polar amino acid within CDR3 (e.g., at position 106) of IGHV3-20, and (b) an acidic amino acid substituted for an uncharged polar amino acid within CDR3 (e.g., at position 108) of IGKV3-20. Changes in the charge display at the CDR surface is expected to affect the antibody's interface with the solvent, and thus create unpredictable conditions for maintaining or advancing the stability of the antibody in solution.

According to certain embodiments of the present invention, the anti-human Ang-2 antibody, or antigen-binding fragment thereof, comprises a heavy chain complementary determining region (HCDR) 1 of SEQ ID NO: 4, an HCDR2 of SEQ ID NO: 6, and an HCDR3 of SEQ ID NO: 8. In certain embodiments, the anti-human Ang-2 antibody, or antigen-binding fragment thereof, comprises an HCVD of SEQ ID NO: 18.

According to certain embodiments of the present invention, the anti-human Ang-2, or antigen-binding fragment thereof, comprises a light (kappa) chain complementary determining region (LCDR) 1 of SEQ ID NO: 12, an LCDR2 of SEQ ID NO: 14, and an LCDR3 of SEQ ID NO: 16. In certain embodiments, the anti-human Ang-2 antibody, or antigen-binding fragment thereof, comprises an LCVD of SEQ ID NO: 20.

The non-limiting, exemplary antibody used in the Examples herein is referred to as "H1H685P", as in US 2011/0027286. This antibody comprises an HCVR/LCVR amino acid sequence pair having SEQ ID NOS: 18/20, and HCDR1-HCDR2-HCDR3/LCDR1-LCDR2-LCDR3 domains represented by SEQ ID NOS: 4-6-8/SEQ ID NOS: 12-14-16.

The amount of antibody, or antigen-binding fragment thereof, contained within the pharmaceutical formulations of the present invention may vary depending on the specific properties desired of the formulations, as well as the particular circumstances and purposes for which the formulations are intended to be used. In certain embodiments, the pharmaceutical formulations are liquid formulations that may contain 5 ± 0.75 mg/mL to 150 ± 22.5 mg/mL of antibody; 7.5 ± 1.125 mg/mL to 140 ± 21 mg/mL of antibody; 10 ± 1.5 mg/mL to 130 ± 19.5 mg/mL of antibody; 12.5 ± 1.875 mg/mL to 120 ± 18 mg/mL of antibody; 15 ± 2.25 mg/mL to 110 ± 16.5 mg/mL of antibody; 17.5 ± 2.625 mg/mL to 100 ± 15 mg/mL of antibody; 20 ± 3 mg/mL to 90 ± 13.5 mg/mL of antibody; 22.5 ± 3.375 mg/mL to 80 ± 12 mg/mL of antibody; 25 ± 3.75 mg/mL to 70 ± 10.5 mg/mL of antibody; 27.5 ± 4.125 mg/mL to 60 ± 9 mg/mL of antibody; 30 ± 4.5 mg/mL to 50 ± 7.5 mg/mL of antibody; 25 ± 3.75 mg/mL of antibody; or 50 ± 7.5 mg/mL. For example, the formulations of the present invention may comprise about 20 mg/mL; about 25 mg/mL; about 30 mg/mL; about 35 mg/mL; about 40 mg/mL; about 45 mg/mL; about 50 mg/mL; about 55 mg/mL; or about 60 mg/mL of an antibody or an antigen-binding fragment thereof, that binds specifically to human Ang-2.

Excipients and pH

The pharmaceutical formulations of the present invention comprise one or more excipients. The term "excipient", as used herein, means any non-therapeutic agent added to the formulation to provide a desired consistency, viscosity or stabilizing effect.

In certain embodiments, the pharmaceutical formulation of the invention comprises at least one organic cosolvent in a type and in an amount that stabilizes the human Ang-2 antibody under conditions of rough handling or agitation, such as, e.g., vortexing. In some embodiments, what is meant by "sta-

bilizes" is the prevention of the formation of more than 4% aggregated antibody of the total amount of antibody (on a molar basis) over the course of rough handling. In some embodiments, rough handling is vortexing a solution containing the antibody and the organic cosolvent for about 60 minutes or about 120 minutes.

In certain embodiments, the organic cosolvent is a non-ionic surfactant, such as an alkyl poly(ethylene oxide). Specific non-ionic surfactants that can be included in the formulations of the present invention include, e.g., polysorbates such as polysorbate 20, polysorbate 28, polysorbate 40, polysorbate 60, polysorbate 65, polysorbate 80, polysorbate 81, and polysorbate 85; poloxamers such as poloxamer 181, poloxamer 188, poloxamer 407; or polyethylene glycol (PEG). Polysorbate 20 is also known as TWEEN 20, sorbitan monolaurate and polyoxyethylenesorbitan monolaurate. Poloxamer 188 is also known as PLURONIC F68.

The amount of non-ionic surfactant contained within the pharmaceutical formulations of the present invention may vary depending on the specific properties desired of the formulations, as well as the particular circumstances and purposes for which the formulations are intended to be used. In certain embodiments, the formulations may contain $0.01\pm0.0015\%$ to $1\pm0.15\%$ surfactant. For example, the formulations of the present invention may comprise about 0.085%; about 0.01%; about 0.02%; about 0.03%; about 0.04%; about 0.05%; about 0.06%; about 0.07%; about 0.08%; about 0.09%; about 0.1%; about 0.11%; about 0.12%; about 0.13%; about 0.14%; about 0.15%; about 0.16%; about 0.17%; about 0.18%; about 0.19%; about 0.20%; about 0.21%; about 0.22%; about 0.23%; about 0.24%; about 0.25%; about 0.3%; about 0.4%; about 0.5%; about 0.6%; about 0.7%; about 0.8%; about 0.9%; about 1%; about 1.1%; about 1.15%; or about 1.2% polysorbate 20 or poloxamer 188.

The pharmaceutical formulations of the present invention may also comprise one or more stabilizers in a type and in an amount that stabilizes the human Ang-2 antibody under conditions of thermal stress. In some embodiments, what is meant by "stabilizes" is maintaining greater than about 93% of the antibody in a native conformation when the solution containing the antibody and the thermal stabilizer is kept at about 45° C. for up to about 28 days. In some embodiments, what is meant by "stabilizes" is wherein less than about 4% of the antibody is aggregated when the solution containing the antibody and the thermal stabilizer is kept at about 45° C. for up to about 28 days. In some embodiments, what is meant by "stabilizes" is maintaining greater than about 96% of the antibody in a native conformation when the solution containing the antibody and the thermal stabilizer is kept at about 37° C. for up to about 28 days. In some embodiments, what is meant by "stabilizes" is wherein less than about 2% of the antibody is aggregated when the solution containing the antibody and the thermal stabilizer is kept at about 37° C. for up to about 28 days. As used herein, "native" means the major form of the antibody by size exclusion, which is generally an intact monomer of the antibody.

In certain embodiments, the thermal stabilizer is a sugar or sugar alcohol selected from sucrose, sorbitol, glycerol, trehalose and mannitol, or any combination thereof, the amount of which contained within the formulation can vary depending on the specific circumstances and intended purposes for which the formulation is used. In certain embodiments, the formulations may contain about 3% to about 20% sugar or sugar alcohol; about 4% to about 19% sugar or sugar alcohol; about 5% to about 18% sugar or sugar alcohol; about 6% to about 17% sugar or sugar alcohol; about 7% to about 16%

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sugar or sugar alcohol; about 8% to about 15% sugar or sugar alcohol; about 9% to about 16% sugar or sugar alcohol; about 7% to about 13% sugar or sugar alcohol; about 8% to about 12% sugar or sugar alcohol; about 9% to about 11% sugar or sugar alcohol; or about 10% sugar or sugar alcohol. For example, the pharmaceutical formulations of the present invention may comprise 4% \pm 0.6%; 5% \pm 0.75%; 6% \pm 0.9%; 7% \pm 1.05%; 8% \pm 1.2%; 9% \pm 1.35%; 10% \pm 1.5%; 11% \pm 1.65%; 12% \pm 1.8%; 13% \pm 1.95%; or about 14% \pm 2.1% sugar or sugar alcohol (e.g., sucrose, trehalose or mannitol).

The pharmaceutical formulations of the present invention may also comprise a buffer or buffer system, which serves to maintain a stable pH and to help stabilize the human Ang-2 antibody. In some embodiments, what is meant by "stabilizes" is wherein less than 5% \pm 0.5% or no more than about 4.3% of the antibody is aggregated when the solution containing the antibody and the buffer is kept at about 45° C. for up to about 28 days. In some embodiments, what is meant by "stabilizes" is wherein at least 92% \pm 0.5% of the antibody is in its native conformation as determined by size exclusion chromatography when the solution containing the antibody and the buffer is kept at about 45° C. for up to about 28 days. By "native" or "native conformation", what is meant is the antibody fraction that is not aggregated or degraded. This is generally determined by an assay that measures the relative size of the antibody entity, such as a size exclusion chromatographic assay. The non-aggregated and non-degraded antibody elutes at a fraction that equates to the native antibody, and is generally the main elution fraction. Aggregated antibody elutes at a fraction that indicates a size greater than the native antibody. Degraded antibody elutes at a fraction that indicates a size less than the native antibody.

In some embodiments, what is meant by "stabilizes" is wherein at least 52% \pm 0.5% of the antibody is in its main charge form as determined by cation exchange chromatography when the solution containing the antibody and the buffer is kept at about 45° C. for up to about 28 days. By "main charge" or "main charge form", what is meant is the fraction of antibody that elutes from an ion exchange resin in the main peak, which is generally flanked by more "basic" peaks on one side and more "acidic" peaks on the other side.

The pharmaceutical formulations of the present invention may have a pH of from about 5.5 to about 6.5. For example, the formulations of the present invention may have a pH of about 5.5; about 5.6; about 5.7; about 5.8; about 5.9; about 6.0; about 6.1; about 6.2; about 6.3; about 6.4; or about 6.5. In some embodiments, the pH is 6.0 \pm 0.4; 6.0 \pm 0.3; 6.0 \pm 0.2; 6.0 \pm 0.1; about 6.0; or 6.0.

In some embodiments, the buffer or buffer system comprises at least one buffer that has a buffering range that overlaps fully or in part the range of pH 5.5-7.4. In one embodiment, the buffer has a pKa of about 6.0 \pm 0.5. In certain embodiments, the buffer comprises a histidine buffer. In certain embodiments, the histidine is present at a concentration of 5 mM \pm 0.75 mM to 15 mM \pm 2.25 mM; 6 mM \pm 0.9 mM to 14 mM \pm 2.1 mM; 7 mM \pm 1.05 mM to 13 mM \pm 1.95 mM; 8 mM \pm 1.2 mM to 12 mM \pm 1.8 mM; 9 mM \pm 1.35 mM to 11 mM \pm 1.65 mM; 10 mM \pm 1.5 mM; or about 10 mM. In certain embodiments, the buffer system comprises histidine at 10 mM \pm 1.5 mM, at a pH of 6.0 \pm 0.3 or 6.4 \pm 0.3.

Exemplary Formulations

According to one aspect of the present invention, the pharmaceutical formulation is a low viscosity, i.e., having a viscosity of under 10 cPoise or about 1.4 \pm 0.21 cPoise, generally physiologically isotonic, i.e., between 300 and 400 mOsm or about 363 \pm 54 mOsm, liquid formulation, which comprises: (i) a human antibody that specifically binds to human Ang-2

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(e.g., H1H685P), at a concentration of 25 mg/mL \pm 3.75 mg/mL, or 50 mg/mL \pm 7.5 mg/mL; (ii) a buffer system that provides sufficient buffering at about pH 6.0 \pm 0.3; (iii) a sugar which serves as a thermal stabilizer; and (iv) an organic cosolvent, which protects the structural integrity if the antibody.

According to one embodiment, the pharmaceutical formulation comprises: (i) a human IgG1 antibody that specifically binds to human Ang-2 and which comprises a substituted IGHV3-13.01 type heavy chain variable region and a substituted IGKV3-20.01 type light chain variable region (e.g., H1H685P) at a concentration from 20 \pm 3 mg/mL to about 60 \pm 9 mg/mL; (ii) a buffer system comprising histidine, which buffers effectively at about pH 6.0 \pm 0.3; (iii) sucrose; and (iv) a non-ionic detergent, such as a polysorbate.

According to one embodiment, the pharmaceutical formulation comprises: (i) a human IgG1 antibody that specifically binds to human Ang-2, and which comprises an HCDR1 of SEQ ID NO: 4, an HCDR2 of SEQ ID NO: 6, an HCDR3 of SEQ ID NO: 8, an LCDR1 of SEQ ID NO: 12, an LCDR2 of SEQ ID NO: 14, and an LCDR3 of SEQ ID NO: 16, at a concentration of 25 mg/ml \pm 3.75 mg/mL; (ii) histidine at 10 mM \pm 1.5 mM, which buffers at pH 6.0 \pm 0.3; (iii) sucrose at 10% w/v \pm 1.5% w/v; and (iv) polysorbate 20 at 0.2% w/v \pm 0.03% w/v.

According to one embodiment, the pharmaceutical formulation comprises: (i) a human IgG1 antibody that specifically binds to human Ang-2, and which comprises an HCDR1 of SEQ ID NO: 4, an HCDR2 of SEQ ID NO: 6, an HCDR3 of SEQ ID NO: 8, an LCDR1 of SEQ ID NO: 12, an LCDR2 of SEQ ID NO: 14, and an LCDR3 of SEQ ID NO: 16, at a concentration of about 50 mg/ml \pm 7.5 mg/mL; (ii) histidine at 10 mM \pm 1.5 mM, which buffers at pH 6.0 \pm 0.3; (iii) sucrose at 10% w/v \pm 1.5% w/v; and (iv) polysorbate 20 at 0.2% w/v \pm 0.03% w/v.

According to one embodiment, the pharmaceutical formulation comprises: (i) a human IgG1 antibody that specifically binds to human Ang-2, and which comprises a heavy chain variable domain of SEQ ID NO: 18, and a light chain variable domain of SEQ ID NO: 20, at a concentration of 25 mg/ml \pm 3.75 mg/mL; (ii) histidine at 10 mM \pm 1.5 mM, which buffers at pH 6.0 \pm 0.3; (iii) sucrose at 10% w/v \pm 1.5% w/v; and (iv) polysorbate 20 at 0.2% w/v \pm 0.03% w/v.

According to one embodiment, the pharmaceutical formulation comprises: (i) a human IgG1 antibody that specifically binds to human Ang-2, and which comprises a heavy chain variable domain of SEQ ID NO: 18, and a light chain variable domain of SEQ ID NO: 20, at a concentration of about 50 mg/ml \pm 7.5 mg/mL; (ii) histidine at 10 mM \pm 1.5 mM, which buffers at pH 6.0 \pm 0.3; (iii) sucrose at 10% w/v \pm 1.5% w/v; and (iv) polysorbate 20 at 0.2% w/v \pm 0.03% w/v.

Additional non-limiting examples of pharmaceutical formulations encompassed by the present invention are set forth elsewhere herein, including the working Examples presented below.

Stability and Viscosity of the Pharmaceutical Formulations

The pharmaceutical formulations of the present invention typically exhibit high levels of stability. The term "stable", as used herein in reference to the pharmaceutical formulations, means that the antibodies within the pharmaceutical formulations retain an acceptable degree of chemical structure or biological function after storage under defined conditions. A formulation may be stable even though the antibody contained therein does not maintain 100% of its chemical structure or biological function after storage for a defined amount of time. Under certain circumstances, maintenance of about 90%, about 95%, about 96%, about 97%, about 98% or about

99% of an antibody's structure or function after storage for a defined amount of time may be regarded as "stable".

Stability can be measured, inter alia, by determining the percentage of native antibody that remains in the formulation after storage for a defined amount of time at a defined temperature. The percentage of native antibody can be determined by, inter alia, size exclusion chromatography (e.g., size exclusion high performance liquid chromatography [SE-HPLC]), such that native means non-aggregated and non-degraded. An "acceptable degree of stability", as that phrase is used herein, means that at least 90% of the native form of the antibody can be detected in the formulation after storage for a defined amount of time at a given temperature. In certain embodiments, at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% of the native form of the antibody can be detected in the formulation after storage for a defined amount of time at a defined temperature. The defined amount of time after which stability is measured can be at least 14 days, at least 28 days, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least 18 months, at least 24 months, or more. The defined temperature at which the pharmaceutical formulation may be stored when assessing stability can be any temperature from about -80° C. to about 45° C., e.g., storage at about -80° C., about -30° C., about -20° C., about 0° C., about 4°-8° C., about 5° C., about 25° C., about 35° C., about 37° C., or about 45° C. For example, a pharmaceutical formulation may be deemed stable if after nine months of storage at 5° C., greater than about 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after six months of storage at 25° C., greater than about 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 37° C., greater than about 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 45° C., greater than about 93%, 94%, 95%, 96%, 97%, 98% or 99% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after six months of storage at -20° C., greater than about 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after six months of storage at -30° C., greater than about 96%, 96.5%, 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC. A pharmaceutical formulation may also be deemed stable if after six months of storage at -80° C., greater than about 97%, 97.5%, 98%, 98.5%, 99% or 99.5% of native antibody is detected by SE-HPLC.

Stability can be measured, inter alia, by determining the percentage of antibody that forms in an aggregate within the formulation after storage for a defined amount of time at a defined temperature, wherein stability is inversely proportional to the percent aggregate that is formed. The percentage of aggregated antibody can be determined by, inter alia, size exclusion chromatography (e.g., size exclusion high performance liquid chromatography [SE-HPLC]). An "acceptable degree of stability", as that phrase is used herein, means that at most 6% of the antibody is in an aggregated form detected in the formulation after storage for a defined amount of time at a given temperature. In certain embodiments an acceptable degree of stability means that at most about 6%, 5%, 4%, 3%,

2%, 1%, 0.5%, or 0.1% of the antibody can be detected in an aggregate in the formulation after storage for a defined amount of time at a given temperature. The defined amount of time after which stability is measured can be at least 2 weeks, at least 28 days, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least 18 months, at least 24 months, or more. The temperature at which the pharmaceutical formulation may be stored when assessing stability can be any temperature from about -80° C. to about 45° C., e.g., storage at about -80° C., about -30° C., about -20° C., about 0° C., about 4°-8° C., about 5° C., about 25° C., about 35° C., about 37° C. or about 45° C. For example, a pharmaceutical formulation may be deemed stable if after nine months of storage at 5° C., less than about 2%, 1.75%, 1.5%, 1.25%, 1%, 0.75%, 0.5%, 0.25%, or 0.1% of the antibody is detected in an aggregated form. A pharmaceutical formulation may also be deemed stable if after six months of storage at 25° C., less than about 2%, 1.75%, 1.5%, 1.25%, 1%, 0.75%, 0.5%, 0.25%, or 0.1% of the antibody is detected in an aggregated form. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 45° C., less than about 4%, 3.5%, 3%, 2.5%, 2%, 1.5%, 1%, 0.5%, or 0.1% of the antibody is detected in an aggregated form. A pharmaceutical formulation may also be deemed stable if after three months of storage at -20° C., -30° C., or -80° C. less than about 2%, 1.9%, 1.8%, 1.7%, 1.6%, 1.5%, 1%, 0.5%, or 0.1% of the antibody is detected in an aggregated form.

Stability can be measured, inter alia, by determining the percentage of antibody that migrates in a more acidic fraction during ion exchange ("acidic form") than in the main fraction of antibody ("main charge form"), wherein stability is inversely proportional to the fraction of antibody in the acidic form. While not wishing to be bound by theory, deamidation of the antibody may cause the antibody to become more negatively charged and thus more acidic relative to the non-deamidated antibody (see, e.g., Robinson, N., Protein Deamidation, PNAS, Apr. 16, 2002, 99(8):5283-5288). The percentage of "acidified" antibody can be determined by ion exchange chromatography (e.g., cation exchange high performance liquid chromatography [CEX-HPLC]). An "acceptable degree of stability", as that phrase is used herein, means that at most 52% of the antibody is in a more acidic form detected in the formulation after storage for a defined amount of time at a defined temperature. In certain embodiments an acceptable degree of stability means that at most about 52%, 50%, 45%, 40%, 35%, 30%, 29%, 28%, 27%, 26%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1%, 0.5%, or 0.1% of the antibody can be detected in an acidic form in the formulation after storage for a defined amount of time at a given temperature. The defined amount of time after which stability is measured can be at least 2 weeks, at least 28 days, at least 1 month, at least 2 months, at least 3 months, at least 4 months, at least 5 months, at least 6 months, at least 7 months, at least 8 months, at least 9 months, at least 10 months, at least 11 months, at least 12 months, at least 18 months, at least 24 months, or more. The temperature at which the pharmaceutical formulation may be stored when assessing stability can be any temperature from about -80° C. to about 45° C., e.g., storage at about -80° C., about -30° C., about -20° C., about 0° C., about 4°-8° C., about 5° C., about 25° C., or about 45° C. For example, a pharmaceutical formulation may be deemed stable if after three months of storage at -80° C., -30° C., or -20° C. less than about 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%,

17%, 16%, 15%, 14%, 13%, 12%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5% or 0.1% of the antibody is in a more acidic form. A pharmaceutical formulation may also be deemed stable if after nine months of storage at 5° C., less than about 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5% or 0.1% of the antibody is in a more acidic form. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 25° C., less than about 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5% or 0.1% of the antibody is in a more acidic form. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 37° C., less than about 37%, 36%, 35%, 34%, 33%, 32%, 31%, 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5% or 0.1% of the antibody is in a more acidic form. A pharmaceutical formulation may also be deemed stable if after 28 days of storage at 45° C., less than about 52%, 51%, 50%, 49%, 48%, 47%, 46%, 45%, 44%, 43%, 42%, 41%, 40%, 39%, 38%, 37%, 36%, 35%, 34%, 33%, 32%, 31%, 30%, 29%, 28%, 27%, 26%, 25%, 24%, 23%, 22%, 21%, 20%, 19%, 18%, 17%, 16%, 15%, 14%, 13%, 12%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.5% or 0.1% of the antibody can be detected in a more acidic form.

Measuring the binding affinity of the antibody to its target may also be used to assess stability. For example, a formulation of the present invention may be regarded as stable if, after storage at e.g., -80° C., -30° C., -20° C., 5° C., 25° C., 37° C., 45° C., etc. for a defined amount of time (e.g., 14 days to 6 months), the anti-Ang-2 antibody contained within the formulation binds to Ang-2 with an affinity that is at least 84%, 90%, 95%, or more of the binding affinity of the antibody prior to said storage. Binding affinity may be determined by any method, such as e.g., ELISA or plasmon resonance. Biological activity may be determined by an Ang-2 activity assay, such as by contacting a cell that expresses Ang-2 with the formulation comprising the anti Ang-2 antibody. The binding of the antibody to such a cell may be measured directly, such as via FACS analysis. Alternatively, the downstream activity of the Ang-2 system may be measured in the presence of the antibody, and compared to the activity of the Ang-2 system in the absence of antibody. In some embodiments, the Ang-2 may be endogenous to the cell. In other embodiments, the Ang-2 may be ectopically expressed (i.e., heterologous expression) in the cell.

Additional methods for assessing the stability of an antibody in formulation are demonstrated in the Examples presented below.

Containers and Methods of Administration

The pharmaceutical formulations of the present invention may be contained within any container suitable for storage or administration of medicines and other therapeutic compositions. For example, the pharmaceutical formulations may be contained within a sealed and sterilized plastic or glass container having a defined volume such as a vial, ampule, syringe, cartridge, bottle, or IV bag. Different types of vials can be used to contain the formulations of the present invention including, e.g., clear and opaque (e.g., amber) glass or plastic vials. Likewise, any type of syringe can be used to contain or administer the pharmaceutical formulations of the present invention.

The pharmaceutical formulations of the present invention may be contained within "normal tungsten" syringes or "low tungsten" syringes. As will be appreciated by persons of

ordinary skill in the art, the process of making glass syringes generally involves the use of a hot tungsten rod which functions to pierce the glass thereby creating a hole from which liquids can be drawn and expelled from the syringe. This process results in the deposition of trace amounts of tungsten on the interior surface of the syringe. Subsequent washing and other processing steps can be used to reduce the amount of tungsten in the syringe. As used herein, the term "normal tungsten" means that the syringe contains greater than or equal to 500 parts per billion (ppb) of tungsten. The term "low tungsten" means that the syringe contains less than 500 ppb of tungsten. For example, a low tungsten syringe, according to the present invention, can contain less than about 490, 480, 470, 460, 450, 440, 430, 420, 410, 390, 350, 300, 250, 200, 150, 100, 90, 80, 70, 60, 50, 40, 30, 20, 10 or fewer ppb of tungsten.

The rubber plungers used in syringes, and the rubber stoppers used to close the openings of vials, may be coated to prevent contamination of the medicinal contents of the syringe or vial, or to preserve their stability. Thus, pharmaceutical formulations of the present invention, according to certain embodiments, may be contained within a syringe that comprises a coated plunger, or within a vial that is sealed with a coated rubber stopper. For example, the plunger or stopper may be coated with a fluorocarbon film. Examples of coated stoppers or plungers suitable for use with vials and syringes containing the pharmaceutical formulations of the present invention are mentioned in, e.g., U.S. Pat. Nos. 4,997,423; 5,908,686; 6,286,699; 6,645,635; and 7,226,554, the contents of which are incorporated by reference herein in their entireties. Particular exemplary coated rubber stoppers and plungers that can be used in the context of the present invention are commercially available under the tradename "FluroTec®", available from West Pharmaceutical Services, Inc. (Lionville, Pa.). FluroTec® is an example of a fluorocarbon coating used to minimize or prevent drug product from adhering to the rubber surfaces.

According to certain embodiments of the present invention, the pharmaceutical formulations may be contained within a low tungsten syringe that comprises a fluorocarbon-coated plunger.

The pharmaceutical formulations can be administered to a patient by parenteral routes such as injection (e.g., subcutaneous, intravenous, intramuscular, intraperitoneal, etc.) or 45 percutaneous, mucosal, nasal, pulmonary or oral administration. Numerous reusable pen or autoinjector delivery devices can be used to subcutaneously deliver the pharmaceutical formulations of the present invention. Examples include, but are not limited to AUTOPEN™ (Owen Mumford, Inc., Woodstock, UK), DISETRONIC™ pen (Disetronic Medical Systems, Bergdorf, Switzerland), HUMALOG MIX 75/25™ pen, HUMALOG™ pen, HUMALIN 70/30™ pen (Eli Lilly and Co., Indianapolis, Ind.), NOVOPEN™ I, II and III (Novo Nordisk, Copenhagen, Denmark), NOVOOPEN JUNIOR™ 55 (Novo Nordisk, Copenhagen, Denmark), BD™ pen (Becton Dickinson, Franklin Lakes, N.J.), OPTIPEN™, OPTIPEN PRO™, OPTIPEN STARLET™, and OPTICLIK™ (sanofi-aventis, Frankfurt, Germany). Examples of disposable pen or autoinjector delivery devices having applications in subcutaneous delivery of a pharmaceutical composition of the present invention include, but are not limited to the SOLOSTAR™ pen (sanofi-aventis), the FLEXPEN™ (Novo Nordisk), and the KWIKPENT™ (Eli Lilly), the SURECLICK™ Autoinjector (Amgen, Thousand Oaks, Calif.), the PENLET™ (Haselmeier, Stuttgart, Germany), the EPIPEN (Dey, L. P.), and the HUMIRAT™ Pen (Abbott Labs, Abbott Park, Ill.).

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The use of a microinfusor to deliver the pharmaceutical formulations of the present invention is also contemplated herein. As used herein, the term "microinfusor" means a subcutaneous delivery device designed to slowly administer large volumes (e.g., up to about 2.5 mL or more) of a therapeutic formulation over a prolonged period of time (e.g., about 10, 15, 20, 25, 30 or more minutes). See, e.g., U.S. Pat. No. 6,629,949; U.S. Pat. No. 6,659,982; and Meehan et al., *J. Controlled Release* 46:107-116 (1996). Microinfusors are particularly useful for the delivery of large doses of therapeutic proteins contained within high concentration (e.g., about 100, 125, 150, 175, 200 or more mg/mL) or viscous solutions.

In one embodiment, the pharmaceutical formulation is administered via an IV drip, such that the formulation is diluted in an IV bag containing a physiologically acceptable solution. In one embodiment, pharmaceutical composition is a compounded sterile preparation in an intravenous infusion bag, such that a single dose of drug product is diluted into 100 mL, 250 mL (or other like amount suitable for intravenous drip delivery) of a physiological buffer (e.g., 0.9% saline). In some embodiments, the infusion bag is made of a polyvinyl chloride (e.g., VIAFLEX, Baxter, Deerfield, Ill.). In some embodiments, the infusion bag is made of a polyolefin (EX-CEL IV Bags, Braun Medical Inc., Bethlehem, Pa.).

Therapeutic Uses of the Pharmaceutical Formulations

The pharmaceutical formulations of the present invention are useful, inter alia, for the treatment, prevention or amelioration of any disease or disorder associated with Ang-2 activity, including diseases or disorders mediated by Ang-2. Exemplary, non-limiting diseases and disorders that can be treated or prevented by the administration of the pharmaceutical formulations of the present invention include various diseases involving angiogenesis, which is the biological process whereby new blood vessels are formed. Aberrant angiogenesis is associated with several disease conditions including, e.g., proliferative retinopathies, rheumatoid arthritis and psoriasis. In addition, it is well established that angiogenesis is critical for tumor growth and maintenance.

EXAMPLES

The following examples are presented so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use the methods and compositions of the invention, and are not intended to limit the scope of what the inventors regard as their invention. Efforts have been made to ensure accuracy with respect to numbers used (e.g., amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by mole, molecular weight is average molecular weight, temperature is in degrees Centigrade, and pressure is at or near atmospheric pressure.

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Initial formulation development activities involved empirical experiments and screening organic cosolvents, thermal stabilizers, and buffers in liquid and lyophilized formulations of anti-Ang-2 antibodies to identify excipients that are compatible with the protein and enhance its stability, while maintaining near physiologic osmolality and low viscosity for intravenous and subcutaneous injection. Buffer conditions were also examined to determine the optimal pH for maximum protein stability.

Example 1

Development of Anti-Ang-2 Formulation

Formulation development activities included the screening of buffers, organic cosolvents, and thermal stabilizers in liquid formulations of the anti-Ang-2 antibody to identify excipients that enhance the stability of the protein. Buffer conditions were also examined to determine the optimal pH for maximum protein stability. Results generated from these studies were used to develop a stable, liquid formulation suitable for clinical use. Anti-Ang-2 (e.g., H1H685P) was formulated at 25 ± 3.75 mg/ml and 50 ± 7.5 mg/ml. In one embodiment, the anti-Ang-2 antibody is formulated in 10 ± 1.5 mM histidine (pH 6.0 ± 0.3), $0.2\%\pm0.03\%$ polysorbate 20, $10\%\pm1.5\%$ sucrose.

Example 2

Buffer and pH

The effect of pH and buffer type on the stability of anti-Ang-2 was considered. H1H685P at 25 mg/mL was incubated at 45°C . in either acetate (pH 5.0-5.5), citrate (pH 5.5-6.0), succinate (pH 6.0), histidine (pH 5.5-6.5), phosphate (pH 6.0-8.0), or Tris (pH 8.0) buffer to assess the effect of buffer and pH on the thermal stability of the protein (Table 1). Analysis of protein stability by size exclusion chromatography (SE-HPLC) revealed that acetate (pH 5.5), phosphate (pH 6.0), histidine (pH 5.5-6.5), and succinate performed better than the other buffer systems for the formulation of H1H685P. Maximum protein stability, as determined by cationic exchange chromatography (CEX HPLC), was observed when H1H685P was formulated in histidine buffer at pH 6.0. These analyses also revealed that degradation for the antibody resulted mostly in the formation of aggregates, cleavage products, and charge variants. The optimal pH for H1H685P stability in histidine buffer was observed to be 6.0, although good stability was observed in the pH range of 5.5 to 6.5. Based on these results, 10 mM histidine buffer at pH 6.0 was chosen for the formulation of antibody drug product (DP).

TABLE 1

Effect of Buffer and pH on Stability of H1H685P Incubated at 45°C . for 28 Days							
pH/Buffer	OD _{405¹}	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
Starting Material ²	0.00	100	96.4	2.5	59.6	28.9	11.5
pH 8.0, Tris	0.25	95	73.0	20.7	5.8	89.2	5.1
pH 8.0, Phosphate	0.54	95	52.7	40.2	2.4	94.0	3.6
pH 7.5, Phosphate	0.33	97	66.5	27.8	5.3	94.7	0.0

TABLE 1-continued

Effect of Buffer and pH on Stability of H1H685P Incubated at 45° C. for 28 Days							
pH/Buffer	OD 405 ¹	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
pH 7.0, Phosphate	0.05	101	85.5	10.8	16.8	77.5	5.7
pH 6.5, Phosphate	0.01	100	90.1	6.1	26.0	67.0	7.0
pH 6.0, Phosphate	0.00	100	92.3	4.0	31.0	57.5	11.5
pH 6.5, Histidine	0.01	100	92.6	4.3	31.5	58.7	9.8
pH 6.0, Histidine	0.01	100	92.3	4.3	34.9	52.2	13.0
pH 5.5, Histidine	0.00	100	92.4	4.0	33.1	50.4	16.5
pH 6.0, Succinate	0.00	99	92.3	4.5	32.3	56.4	11.4
pH 6.0, Citrate	0.03	100	89.3	7.4	31.1	57.6	11.3
pH 5.5, Citrate	0.05	100	88.6	8.0	27.3	58.7	14.1
pH 5.5, Acetate	0.00	101	92.8	3.5	32.5	54.3	13.2
pH 5.0, Acetate	0.00	100	91.6	3.7	29.5	52.1	18.4

For the results shown in Table 1, 0.35 mL of 25 mg/mL H1H685P in 10 mM test buffer in a 2 mL Type 1 borosilicate glass vial with a FluroTec® coated 4432/50 butyl rubber stopper were tested for 28 days at 45.¹ Turbidity was reported as the relative change in OD at 405 nm as compared to the starting material.² SE-HPLC and CEX-HPLC Starting Material Results were the average of the starting material for all 14 formulations. OD=Optical density; RP-HPLC=Reverse phase high performance liquid chromatography; SE-HPLC=Size exclusion high performance liquid chromatography; CEX-HPLC=cation exchange high performance liquid chromatography.

Example 3

Selection of Protectants Against Agitation Stress

The H1H685P anti-Ang-2 antibody (i.e., Drug Substance or “DS”) exhibited limited stability when subjected to agitation stress. Turbidity analysis of agitated DS demonstrated an increase in optical density (OD) at 405 nm when H1H685P was vortexed for 120 minutes (Table 2, see No Cosolvent data). This increase in turbidity indicates a significant formation of particulates as a result of the agitation stress. Agitation of the formulation in the absence of cosolvent also resulted in a significant increase in aggregate formation. Formulation with any of the evaluated cosolvents prevented the agitation

dependent increase in turbidity and aggregate levels of H1H685P (Table 2). However, the addition of 0.2% PLURONIC F68, 20% PEG 300, 10% PEG 300, and 20% propylene glycol to the formulation significantly decreased the thermal stability of H1H685P as determined by SE-HPLC and CEX-HPLC (Table 3). Formulations containing polysorbate 20, polysorbate 80, and PEG 3350 had no significant effect on the thermal stability of H1H685P as determined by SE-HPLC and CEX-HPLC, making these cosolvents suitable for the formulation of H1H685P (Table 3). Polysorbate 20 was chosen as the organic cosolvent for development of a H1H685P formulation because it stabilized the protein to agitation stress, had no effect on its thermal stability, and required lower co-solvent concentrations to stabilize the protein compared to polyethylene glycol.

For the antibody stability results shown in Table 2, 0.8 mL of 5 mg/mL H1H685P, in 10 mM histidine, pH 6.0 to 6.1 in a 2 mL Type 1 borosilicate glass vial with a FluroTec® coated 4432/50 butyl rubber stopper was combined with the organic cosolvents and subjected to 120 minutes of vortexing.¹ Turbidity was reported as the relative change in OD at 405 nm as compared to the starting material.² SE-HPLC and CEX-HPLC Starting Material Results were the average of the starting material for all nine formulations. OD=Optical density; RP-HPLC=Reverse phase high performance liquid chromatography; SE-HPLC=Size exclusion high performance liquid chromatography.

TABLE 2

Effect of Organic Cosolvents on Antibody Stability - Agitation							
Organic Cosolvent	OD 405 ¹	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
Starting Material ² (no vortexing)	0.00	100	98.3	0.6	59.3	32.8	7.9
No Cosolvent	0.25	103	76.6	22.3	60.4	30.9	8.7
0.2% Polysorbate 20	0.00	99	98.3	0.6	59.5	32.9	7.7
0.2% Polysorbate 80	0.00	99	98.2	0.6	59.4	32.8	7.8
0.2% Pluronic F68	0.00	98	98.3	0.7	59.4	32.7	7.9
3.0% PEG 3350	0.00	96	98.6	0.6	59.4	32.9	7.7
1.0% PEG 3350	0.00	99	98.3	0.7	59.7	32.8	7.6

TABLE 2-continued

Effect of Organic Cosolvents on Antibody Stability - Agitation							
Organic Cosolvent	OD 405 ¹	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
20% PEG 300	0.01	101	98.1	0.8	57.6	33.1	9.3
10% PEG 300	0.01	100	97.9	0.9	59.0	32.7	8.2
20% Propylene Glycol	0.00	101	98.1	0.8	59.7	32.5	7.8

TABLE 3

Effect of Organic Cosolvents on Antibody Stability - Thermal							
Organic Cosolvent	OD 405 ¹	% Total (RP)	% Native (SE)	% Aggreg. (SE)	% Main Peak (CEX)	% Acidic Peak (CEX)	% Basic Peak (CEX)
Starting Material ² (no incubation)	0.00	100	98.3	0.6	59.3	32.8	7.9
No Cosolvent	0.01	97	95.3	0.7	35.1	53.8	7.3
0.2% Polysorbate 20	0.01	97	95.3	0.7	34.9	53.7	7.4
0.2% Polysorbate 80	0.01	97	95.1	0.9	34.9	53.8	7.5
0.2% Pluronic F68	0.01	96	95.1	0.6	31.2	53.1	9.3
3.0% PEG 3350	0.01	96	95.7	0.8	35.0	52.4	7.9
1.0% PEG 3350	0.01	96	96.0	0.7	35.5	52.7	7.6
20% PEG 300	0.12	103	71.5	5.0	5.1	81.5	0.0
10% PEG 300	0.06	100	91.6	1.5	5.6	76.6	0.0
20% Propylene Glycol	0.00	98	92.2	0.8	34.3	52.5	8.2

For the antibody stability results shown in Table 3, 0.35 mL of 5 mg/mL H1H685P, in 10 mM histidine, pH 6.0 to 6.1 in a 2 mL Type 1 borosilicate glass vial with a FluroTec® coated 4432/50 butyl rubber stopper was combined with the organic cosolvents and subjected to 45° C. for 28 days.¹ Turbidity was reported as the relative change in OD at 405 nm as compared to the starting material.² SE-HPLC and CEX-HPLC Starting Material Results were the average of the starting material for all nine formulations. OD=Optical density; RP=Reverse phase high performance liquid chromatography; SE=Size exclusion high performance liquid chromatography; CEX=cation exchange high performance liquid chromatography.

Example 4

Selection of Protectants Against Thermal Stress

Stabilizers such as sugars, amino acids, and inorganic salts were examined for their ability to increase the thermal stability of H1H685P. A summary of the thermal stabilizers that were examined is presented in Table 4. Formulations containing 20% sucrose, 10% mannitol, and 20% trehalose had the least amount of H1H685P degradation as determined by SE-HPLC and CEX-HPLC analysis following thermal stress. However, formulation with mannitol destabilized the protein

to multiple freezing and thawing cycles. H1H685P had similar stability to thermal stress when formulated with sucrose or trehalose. Sucrose was chosen as the thermal stabilizer for development of a liquid H1H685P formulation.

H1H685P exhibited maximal stability when formulated in the presence of histidine, polysorbate 20, and sucrose at pH 6.0. 10% sucrose was chosen for the H1H685P DP formulation, which is close to iso-osmolar. The main degradation pathways identified during the development of the H1H685P liquid formulation were the formation of aggregates, cleavage products, and charge variants, with the highest rate of degradation (increase in charge variants) being observed when the protein was incubated at 45° C.

For the antibody stability results shown in Table 4, 0.35 mL of 10 mM Histidine, pH 6.0 to 6.2, 0.2% Polysorbate 20, and 25 mg/mL H1H685P, plus the indicated thermal stabilizer, in a 2 mL Type 1 borosilicate glass vial with a FluroTec® coated 4432/50 butyl rubber stopper were subjected to 45° C. for 28 days.¹ Turbidity was reported as the relative change in OD at 405 nm as compared to the starting material.² SE-HPLC and CEX-HPLC Starting Material Results represents the average values of the starting material for all ten formulations not incubated at 45° C. OD=Optical density; RP=Reverse phase high performance liquid chromatography; SE=Size exclusion high performance liquid chromatography; CEX=cation exchange high performance liquid chromatography.

TABLE 4

Effect of Thermal Stabilizers on the Stability							
Thermal Stabilizer	OD 405 nm ¹	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
Starting Material ²	0.00	100	97.7	1.5	58.7	31.5	9.8
No Stabilizer	0.02	100	92.9	3.7	32.0	55.2	12.8
150 mM NaCl	0.11	101	79.6	17.5	35.4	50.1	14.4

TABLE 4-continued

Effect of Thermal Stabilizers on the Stability							
Thermal Stabilizer	OD 405 nm ¹	% Total (RP-HPLC)	% Native (SE-HPLC)	% Aggregate (SE-HPLC)	% Main Peak (CEX-HPLC)	% Acidic Peak (CEX-HPLC)	% Basic Peak (CEX-HPLC)
10% Sucrose	0.01	100	93.9	2.7	32.7	54.3	13.0
20% Sucrose	0.01	101	94.2	2.4	33.5	53.4	13.2
20% Sorbitol	0.10	101	94.4	1.9	24.5	62.7	12.9
10% Mannitol	0.01	99	94.4	2.3	33.1	53.1	13.8
20% Trehalose	0.01	100	94.7	2.0	33.6	52.9	13.6
5% Glycerol	0.09	103	88.0	8.1	4.7	92.1	3.1
3% Arginine	0.05	99	83.0	13.5	35.2	46.4	18.5
3% Glycine	0.01	102	93.7	3.0	29.1	58.2	12.7

Example 5

Stable Liquid Pharmaceutical Formulation

In conclusion, H1H685P DP was produced as a liquid in an optimized, aqueous buffered formulation containing 10 mM histidine, pH 6.0, 0.2% (w/v) polysorbate 20, 10% (w/v) sucrose, and 25 mg/mL H1H685P. H1H685P DP at 25 mg/mL was physically and chemically stable when subjected to various stress conditions (Table 5). There was no effect on pH, appearance, turbidity, or the amount of H1H685P recovered when the DP was vortexed, frozen and thawed multiple times, or incubated at 25° C. for 14 days. After 28 days of incubation at 37° C., the DP was 0.6% more degraded relative to a control, unstressed sample, as determined by SE-HPLC analysis and 10.1% more degraded (decrease in % main peak) as determined by CEX-HPLC analysis. After 28 days of incubation at 45° C., the DP was 3.6% more degraded compared to unstressed control as determined by SE-HPLC analysis and 23.8% more degraded (decrease in % main peak) as determined by CEX-HPLC analysis. No significant loss of potency, as determined using the H1H685P binding assay described below, was observed for any of the stressed samples.

Potency of the formulated H1H685P was determined by measuring the ability of H1H685P to block the binding of a human angiopoietin-2-His-tagged fusion protein (hAng2-His) to a plate coated with a human Tie2-murine Fc-fusion protein (hTie2-mFc) via a competition sandwich ELISA (the binding assay). hAng2-His was titrated with varying amounts of H1H685P. hAng2-His concentration was calculated assuming a monomeric molecular weight of 50.1 kDa. The ligand-antibody complexes were incubated for 1 hour at 25° C. before transfer to microtiter plates coated with the hTie2-mFc. After one-hour incubation, the wells were washed and bound hAng2-His was detected with an HRP-conjugated anti-His tag monoclonal antibody. The calculated IC₅₀ value, defined as the concentration of antibody required to block 50% of His-tagged hAng2 to Tie2-mFc, was used as an indicator of blocking potency.

For the antibody stability results shown in Table 5, 0.35 mL of 10 mM Histidine, pH 6.0 to 6.1, 0.2% Polysorbate 20, 10% Sucrose, and 25 mg/mL H1H685P, in a 2 mL Type 1 borosilicate glass vial with a FluroTec® coated 4432/50 butyl rubber stopper was combined with the organic cosolvents and subjected to the various designated stresses.⁴⁰⁵¹ Turbidity was reported as the relative change in OD at 405 nm as compared to the starting material.² The acceptance criteria for the binding assay was 50-150% of reference standard.

TABLE 5

Stress Stability of 25 mg/mL Anti-Ang-2 Antibody										
	Stress Test									
	No Stress		Agitation		45° C. Incubation Length of Stress		37° C. Incubation		25° C. Incubation	
	0 min	60 min	120 min	14 days	28 days	14 days	28 days	14 days	28 days	8 cycles
OD 405 nm ¹	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
% Total (RP-HPLC)	100	100	99	101	103	101	103	101	102	97
% Native (SE-HPLC)	97.0	97.1	96.9	95.6	93.4	96.6	96.4	96.8	97.1	96.8
% Aggregate (SE-HPLC)	1.9	1.9	1.9	1.8	3.5	1.6	1.7	1.6	1.7	1.6
% Main Peak (CEX-HPLC)	56.0	56.1	55.9	42.8	32.2	50.4	45.9	55.1	53.5	55.7
% Acidic Peak (CEX-HPLC)	27.0	26.9	27.0	39.2	51.5	30.8	37.0	27.3	29.1	27.2
% Basic Peak (CEX-HPLC)	17.0	17.0	17.1	18.0	16.3	18.8	17.1	17.7	17.4	17.1
Binding Assay ² (% Relative Potency)	105	NP	111	NP	99	NP	122	NP	107	110

25

OD=Optical density; RP=Reverse phase high performance liquid chromatography; SE=Size exclusion high performance liquid chromatography; CEX=cation exchange high performance liquid chromatography.

Example 6

Stability of Formulated Anti-Ang-2 Antibody

Stability studies were performed to determine both the storage and stress stability of the anti-Ang-2 antibody formulation containing 25 mg/mL antibody, 10 mM histidine, pH 6.0 ± 0.3 , 0.2% polysorbate 20, and 10% sucrose. Turbidity and RP-HPLC assays were used to assess the physical stability of the antibody. Physical stability is defined as the recovery of soluble forms of the anti-Ang-2 antibody in solution. Loss of protein could be due to either protein precipitation or surface adsorption. The presence of particulates in solution can be detected by visual inspection or by optical density (OD) measurements at 405 nm (turbidity measurements). In this latter assay, an increase in OD indicates an increase in turbidity due to the formation of particulates. The presence of particulates as determined by OD measurements indicates that the sample has failed to maintain stability. Recovery of antibody is measured by RP-HPLC. In the RP-HPLC assay, the anti-Ang-2 antibody is eluted from the reverse phase column as a single peak. The concentration of each test sample is determined from the area of the eluted antibody peak compared to a calibration curve generated using antibody standards of defined protein loads.

Chemical stability refers to the integrity of the chemical structure of the anti-Ang-2 antibody in a sample. Most chemical instability can be attributed to the formation of covalently modified forms of the antibody, (e.g. covalent aggregates, cleavage products, or charge variants) and non-covalently modified forms of the antibody (e.g. non-covalent aggregates). Thus far, the only degradation products of H1H685P that have been detected are species that differ in either molecular weight or charge. The higher and lower molecular weight degradation products can be separated from native antibody by SE-HPLC. The percentage of native in the size exclusion chromatographic method is determined by the ratio of the area of the native peak to the total area of all anti-Ang-2 antibody peaks.

Charge variant forms of the anti-Ang-2 antibody were resolved from native antibody using cation exchange chromatography. Peaks that eluted from the CEX-HPLC column with retention times earlier than that of the main peak were labeled "Acidic Peaks", while those that eluted from the CEX-HPLC column with retention times later than that of the main peak were labeled "Basic Peaks". The percentage of degraded anti-Ang-2 antibody in the cation exchange chromatographic method is determined by the change in the relative percentage of the main, acidic, and basic peak areas compared to the total area of all anti-Ang-2 antibody peaks.

Evaluation of the antibody under accelerated conditions was performed by subjecting the antibody to a variety of stress tests. These tests represent the extreme handling conditions that the formulated drug substance may be subjected to during the manufacture, storage, or transportation of drug product. The formulated anti-Ang-2 antibody was filled in 5 mL polycarbonate vials for the agitation, cycles of freeze/thaw, and frozen storage conditions. The formulated antibody was filled in glass vials to examine stress stability at high temperatures.

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Example 7

Storage Stability

5 No change was observed in the physical and chemical stability of the 25 mg/mL H1H685P antibody formulation containing 10 mM histidine, pH 6.0 ± 0.3 , 0.2% polysorbate 20, and 10% sucrose, when stored for six months at -80°C ., -30°C ., -20°C ., and 5°C ., and for nine months at 5°C . A slight diminution in binding activity (ELISA competition assay described above) was observed at 6 months at -80°C ., -30°C ., and -20°C ., i.e., ~86%, ~84%, and ~91% of baseline, respectively. See Table 6.

15

Example 8

Stress Stability

20 The stress stability of the 25 mg/mL anti-Ang-2 antibody (H1H685P) formulated in 10 mM histidine, pH 6.0 ± 0.3 , 0.2% polysorbate 20, 10% sucrose was discerned by subjecting the formulation to agitation, thermal stress (45°C ., 37°C ., 25°C .), and freeze thaw stress. The 0.35 mL of the formulation was filled in a 2 mL Type 1 borosilicate glass vial fitted with a FLUROTEC-coated 4432/50 butyl rubber stopper. The results are presented in Table 7.

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Example 9

Molecular Mass Determination

35 A series of analytical, biochemical and biophysical techniques were used to characterize the formulated H1H685P antibody. The molecular weights of the heavy and light chains of glycosylated and deglycosylated H1H685P antibody samples were determined following Capillary Electrophoresis-Sodium Dodecyl Sulfate (CE-SDS) analysis under reducing conditions. Samples were denatured in 0.5% w/v sodium dodecyl sulfate (SDS) and 40 mM dithiothreitol (DTT) at 60°C . for 10 min. Following denaturation and reduction, 1×G7 buffer v/v (1% NONIDET 40 and 50 mM sodium phosphate pH 7.5) was added to the samples. Deglycosylation of H1H685P (50 µg) was accomplished by addition of 1250 units of Peptide N-glycosidase F (PNGase F) and incubation for three hours at 37°C . Untreated control samples were prepared similarly except that the PNGase F enzyme was omitted from the three hour incubation. Samples were desalted following incubation to remove components of the reaction buffer that may interfere with CE-SDS analysis. Desalted samples were completely denatured in 1% w/v SDS and 4.5% w/v β -mercaptoethanol and incubated at 80°C . for 10 min. A 10 kDa molecular weight standard (BECKMAN COULTER) was added to each sample and used as an internal standard to determine peak identity and calculate protein mobility.

TABLE 6

60 Stability of 25 mg/mL H1H685P antibody in 10 mM Histidine, pH 6.0, 0.2% Polysorbate 20, 10% Sucrose					
Storage Condition	$-80^\circ\text{C}.$ / 6 mo.	$-30^\circ\text{C}.$ / 6 mo.	$-20^\circ\text{C}.$ / 6 mo.	$5^\circ\text{C}.$ / 6 mo.	$5^\circ\text{C}.$ / 9 mo.
Appearance	Pass	Pass	Pass	Pass	Pass
pH	6.1	6.1	6.1	6.0	6.1
Turbidity (OD 405 nm) ¹	0.00	0.00	0.00	0.00	0.00

TABLE 6-continued

Stability of 25 mg/mL H1H685P antibody in 10 mM Histidine, pH 6.0, 0.2% Polysorbate 20, 10% Sucrose					
% Total REGN910 Recovered (RP-HPLC)	105	105	107	102	105
Purity by Size-Exclusion-HPLC					
% main peak purity	97.3	96.8	96.8	97.1	96.6
% HMW species	1.8	1.9	1.9	1.8	1.7
Charged Variant Analysis by CE-HPLC					
% region 1 (acidic)	28.3	28.1	27.9	28.1	27.4
% region 2 (main)	55.5	55.9	55.8	55.6	56.3
% region 3 (basic)	16.2	16.0	16.3	16.4	16.2
Binding Assay (% Ref. Std.)	85.95	84.3	90.9	>100	NP

Three principal peaks were observed in the electrophograms of the H1H685P untreated control samples. Peak 1 represents reduced light chain with a calculated molecular weight of approximately 28 kDa (34.0-34.1% total peak area). Peaks 2 and 3 represent non-glycosylated heavy chain (~51 kDa; 3.1-3.8%) and glycosylated heavy chain (~56 kDa; 62.2-62.8% total peak area), respectively. The sum of heavy and light chains (peaks 1, 2, and 3) represent ≥99% of the total percentage of peaks detected by this method for both H1H685P lot samples.

TABLE 7

Stress Stability										
	Stress Test									
	No Stress	Agitation		45° C. Incubation Length of Stress		37° C. Incubation		25° C. Incubation		Freeze/Thaw
		—	60 min	120 min	14 days	28 days	14 days	28 days	14 days	28 days
Appearance	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
pH	6.1	6.0	6.1	6.1	6.2	6.1	6.1	6.0	6.1	6.1
Turbidity (OD at 405 nm)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
% Total REGN910 Recovered (RP-HPLC)	100	100	99	101	103	101	103	101	102	97
Purity by SE- HPLC	97.0	97.1	96.9	95.6	93.4	96.6	96.4	96.8	97.1	96.8
% main peak purity	1.9	1.9	1.9	1.8	3.5	1.6	1.7	1.6	1.7	1.6
% HMW species	27.0	26.9	27.0	39.2	51.5	30.8	37.0	27.3	29.1	27.2
Charged Variant Analysis by CEX-HPLC										
% region 1 (acidic)										
% region 2 (main)	56.0	56.1	55.9	42.8	32.2	50.4	45.9	55.1	53.5	55.7
% region 3 (basic)	17.0	17.0	17.1	18.0	16.3	18.8	17.1	17.7	17.4	17.1
Binding Assay (% Relative Potency)	100	NP	>100	NP	94.3	NP	>100	NP	>100	>100

In the samples treated with PNGase F, there was a substantial decrease in the intensity of peak 3 coupled with a concomitant increase in the intensity of peak 2 in each electropherogram, indicating removal of the glycan chain from the glycosylated heavy chain. The average corrected peak area percentage of peak 2 from the electropherograms generated following capillary electrophoresis of PNGase F treated

H1H685P lot samples (66%) was equivalent to the sum of the mean peak area percentages of peaks 2 and 3 from the electropherograms generated following capillary electrophoresis of the control, non-PNGase F treated samples (66%), indicating complete deglycosylation of the heavy chain following PNGase F incubation. As expected, the molecular weight and relative migration time of the light chain was unchanged.

Multi-angle laser light scattering (MALLS) is an analytical method that provides an estimate of the molecular mass of a protein or glycoprotein. The molar mass of native H1H685P was analyzed by connecting the flow cell of a light scattering detector to a gel filtration column to allow molecular mass analysis of each separated drug substance component (SEC-MALLS). The protein concentration was monitored by differential refractive index and absorbance detectors. Formulated H1H685P lot samples were injected directly onto a TSK Gel G3000SWxl (TOSOH BIOSCIENCES, cat 08541; column dimensions 0.78 cm×30 cm, 5 μm particle size, and porosity of 250 Å), pre-equilibrated in 10 mM sodium phosphate, 500 mM NaCl, pH 6.1 buffer (SEC buffer). The data were analyzed by ASTRA software (WYATT TECHNOLOGY) using the specific refractive index increment, which is defined as the change in refractive index divided by the change in protein concentration (dn/dc), corrected for the high ionic strength of the mobile phase buffer. By SEC-MALLS analysis, the main peak (peak 4, elution volume of ~7.9 mL) for H1H685P corresponded to a molecular weight of approximately 151 kDa. The molar mass identified for the main peak (peak 4) corresponded to intact anti-Ang-2 antibody, which was the predominant species present in solution (96.1-96.9% of the total protein peak area). A very small percentage of two high molecular weight species, corresponding to peak 2 (elution volume of ~6.2 mL) and peak 3

(elution volume of 6.5 mL) and two low molecular weight species, corresponding to peak 5 (elution volume of ~8.4 mL) and peak 6 (elution volume of ~9.8 mL), were detected in all formulated H1H685P samples tested. The calculated molar mass from peak 3 (elution volume of ~6.5 mL) of approximately 300 kDa is consistent with a dimeric form of the H1H685P antibody, and represents a small fraction

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(1.5-1.9%) of the total antibody molecular weight forms present in solution. The calculated molecular weight for peak 5 (elution volume of ~8.4 mL) is approximately 66 kDa and represents 1.5% of the total molecular weight forms present in the sample. Peak 6 represents ~0.2-0.3% of the total peak area. The results from SEC-MALLS analysis of the H1H685P drug substance demonstrated that the majority of the protein exists as an intact antibody with an average molar mass of approximately 151 kDa.

Independent lots of formulated H1H685P were further analyzed to confirm the molecular weight of the intact proteins through mass measurement. 1.5 µg of each protein sample was injected onto a 1.7 µm BEH130 C18 column coupled to a Waters Synapt Mass Spectrometer for mass measurement. The ESI-TOF mass spectra were deconvoluted for the intact proteins using a maximum entropy algorithm with 11 iterations. Based on the heavy and light chain cDNA sequences of H1H685P, the intact antibody (with heavy chain C-terminal Lys removed) was predicted to have a molecular weight of 144604.4 Da. The deconvoluted mass spectra of the intact H1H685P lots showed a similar pattern, with each spectra containing multiple peaks differing by masses of either 146 dalton (fucose) or 162 dalton (galactose), suggesting the presence of glycosylation related micro-heterogeneity. These glycan masses were obtained by subtracting the predicted molecular weight of 144604.4 from the observed intact masses. For example, the 2nd ESI/MS peak has m/z 147493 Da, less of intact MAb MW at 144604.4 Da leaves the glycan mass at 2889 Da. Since the glycans are added on the both sides of Fc, the glycan mass should be 1445 Da.

These glycan masses were used to assign the major H1H685P glycan structural forms. The analysis showed that these glycans are primarily composed of fucosylated complex bi-antennary structures, with 0, 1, and 2 galactoses at the glycan chain termini. The mass difference between the predicted and observed masses (4 Dalton) for the protein amino acid sequence was within the mass accuracy specification of the Synapt MS. These results confirmed the identity of H1H685P at the primary sequence level.

Example 10

Isoelectric Point Determination

H1H685P was analyzed by one-dimensional isoelectric focusing (IEF) under native conditions to determine the isoelectric point (pI) of the intact antibody. A series of pI standards were included in the study, with protein bands visualized by Colloidal blue staining. All sample preparations of H1H685P exhibited a total of eight bands of varying intensity that migrated between a pI of 7.9 and 8.4, with the dominant form having a pI of 8.2. The band migrating at a pI of approximately 8.2, exhibited a slightly lower pI than the predicted pI of 8.6 for the intact antibody. This major band most likely represents fully glycosylated intact antibody lacking the C-terminal lysine (predicted pI of 8.54). This interpretation is consistent with mass spectrometry analysis of the heavy chain following proteolytic digestion and reverse phase separation. In the mass spectrometry analysis, the dominant C-terminal peptide from the H1H685P heavy chain was observed to be lacking the terminal lysine residue, predicted to be present from the cDNA sequence. Three minor basic variants (corresponding to a pI range of 8.3-8.4) were observed. While not wishing to be bound by theory, these minor species may represent partial forms of the antibody, such as an antibody form possessing only heavy chain dimer (predicted pI of 8.9), or heavy chain dimer lacking one or two C-terminal lysines.

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Alternatively, these species may be consistent with a small amount of a charged variant form of the intact antibody containing one or two C-terminal lysines. This interpretation is consistent with the mass spectral analysis of the heavy chain after tryptic digestion and separation of peptides by reverse phase chromatography. Approximately 2.5% of the H1H685P heavy chain was identified by mass spectrometry to contain the C-terminal lysine.

The pI of the native, monomeric form of the kappa light chain from H1H685P is predicted to be 6.4. No band corresponding to a pI of 6.4 was detected under the conditions employed, suggesting that minimal, if any, amounts of free light chain are present in the formulated H1H685P preparation. Although currently unidentified, four additional minor bands that migrated to a more acidic pH relative to the principal band (corresponding to a pI range of 7.9-8.1) were present in all tested samples, and may be speculated to represent intact, glycosylated antibody with deamidated forms, incorrectly formed intermolecular disulfide bonds, or small amounts of truncated forms of the antibody.

The charge heterogeneity of formulated H1H685P was also quantitatively assessed by isoelectric focusing using a capillary electrophoresis (cIEF) based method. For this study, each H1H685P sample was diluted to 0.4 mg/mL (100 µg) in cIEF gel (BECKMAN COULTER, cat 477497) containing 39 mM arginine, 2.3 mM iminodiacetic acid, and 3-10 PHARMALYTES (GE HEALTHCARE; 12 µL). A total of seven peaks of varying intensity were observed ranging from 7.77 to 8.48. The pI range of product related peaks observed by cIEF is slightly greater than the pI range observed by the gel-based isoelectric focusing method (pI range of 7.9-8.4) due to the increased resolution of the capillary. Highly similar qualitative peak patterns were observed from the electropherograms from each DS lot tested. There were a total of four major peaks (peaks 4-7) that represented approximately 92-93% of the total peak area. While not wishing to be bound by theory, these peaks may represent intact antibody lacking the C-terminal lysine, truncated or partial forms of the antibody, non-covalent intact forms of the antibody, or forms with incorrectly formed disulfides. It is possible that some of these peaks may arise during sample preparation or under the electrophoretic conditions employed. Peak 4 represents the dominant charge variant species with a pI of approximately 8.1 and average peak area percentages of 57.5% and 53.4% for each of two formulated H1H685P sample lots tested.

To further examine charge heterogeneity of the H1H685P formulated antibody, several samples were analyzed by two-dimensional gel electrophoresis. For the 2-D gel method, proteins were reduced and then separated on the basis of charge in the first dimension using isoelectric focusing. Subsequently, separated charged species were further resolved in the second dimension based on molecular weight using SDS-PAGE performed under reducing conditions. Each reduced H1H685P sample (2 µg), in the presence or absence of BIO-RAD 2-D pI standards, was loaded onto pH 3-10 immobilized pH gradient (IPG) strips for analysis in the first dimension. Following isoelectric focusing, the IPG strips were loaded onto 4-20% NOVEX Tris glycine gels for analysis in the second dimension. The second dimension was run in the presence of molecular weight standards. In addition, a series of internal standards of known pI were included in the isoelectric focusing analysis. All proteins were visualized by Coomassie Blue staining. Following 2-D gel electrophoresis and protein spot analysis, all H1H685P lot samples exhibited comparable spot patterns, with similar charge variant species present, likely due to equivalent heterogeneity of the heavy chain. A total of three H1H685P-related spots were observed

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in the gel that corresponded to an approximate mass of 55 kDa, with one highly abundant form exhibiting a pI corresponding to approximately 8.2. This spot (pI of ~8.2) is consistent with the reduced, glycosylated heavy chain polypeptide lacking the C-terminal lysine, detected by mass spectrometry analysis. Two unidentified minor spots, detected in the 2-D gel, exhibited isoelectric points between approximately pH 7.5-8.0. In one theoretical scenario, it is possible that these spots consist of assay dependent deamidated protein forms or truncated forms of the heavy chain. Alternatively, it is possible that sample processing or gel artifacts may have led to spot spreading, resulting in the appearance of additional minor spots of varying isoelectric points.

As anticipated, the H1H685P light chain migrated within the 2 D gel as a single major spot, corresponding to a pI of approximately 6.0 with a molecular weight of approximately 25 kDa. An unidentified minor spot (pI of ~5.8) with a molecular weight of about 25 kDa was also observed. This spot may represent a small percentage of deamidated light chain, which was also detected in mass spectrometry analysis.

Example 11

Post-Translational Modifications

Like most IgG1 antibodies, the H1H685P heavy chain terminates with the expected amino acid sequence, Pro-Gly-Lys, with the C-terminal Lys residue susceptible to removal by an unidentified basic carboxypeptidase during protein expression. Partial removal of the terminal Lys could lead to charge heterogeneity within the antibody drug substance. From the peptide mapping analysis of the reduced H1H685P, it was confirmed that the majority of the C-terminal Lys⁴⁵² residue in the tryptic peptide was removed from the heavy chain, resulting in a C-terminal peptide with a sequence of ⁴⁴⁵SLSLSPG⁴⁵¹ (SEQ ID NO: 532). Only a very small percentage of tryptic peptide containing the C-terminal Lys residue (⁴⁴⁵SLSLSPGK⁴⁵²; SEQ ID NO: 533) was observed in the tryptic map. Based on the integrated peak areas of the two tryptic C-terminal heavy chain peptides from each lot of H1H685P, approximately 1.0% and 1.5% of the H1H685P antibody heavy chain contained C-terminal Lys⁴⁵² in the toxicology and clinical lots, respectively.

Non-enzymatic deamidation of asparagine is another common modification that is frequently observed in antibodies. Deamidation, which occurs via the formation of a succinimide intermediate, followed by hydrolysis, results in the formation of isoaspartate and aspartate. Each deamidation event introduces one additional negative charge to an antibody and generates charge heterogeneity. An asparagine residue followed by glycine or serine within the primary amino acid sequence is by far the most susceptible site for deamidation within a protein. In H1H685P, two asparagine residues in the heavy chain (Asn³²⁰ and Asn³⁸⁹) are directly followed by glycine residues and are therefore candidate sites for deamidation. Mass spectrometry analysis indicated that little deamidation occurred at Asn³²⁰ in any of the H1H685P sample lots. Focused mass analysis revealed that Asn³⁸⁹ was identified within a peptide eluted as peak 53. A peptide containing a deamidated form of Asn³⁸⁹ eluted within peak 52. Due to other co-eluting peptides within peak 52, it was not possible to obtain a quantitative analysis of the relative amount of deamidation based on the UV signal. However, using ion intensities from the mass spectra, the relative percentage of deamidated Asn³⁸⁹ in either of the lots of H1H685P was

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determined to be less than 2%. In the reduced peptide map of H1H685P, mass spectrometry analysis also identified peak 49 as a light chain tryptic peptide that contained a native form of asparagine 94 followed by serine. An equivalent peptide, containing a deamidated form of Asn⁹⁴ from the light chain, was also identified (peak 48). Integration of these two peaks revealed that approximately 4.2% of the total amount of this asparagine was present in the deamidated form in both the toxicology and clinical lots. Light chain asparagine 94 was identified as the only Asn-Ser containing peptide that exhibited deamidation end products in H1H685P. The light chain Asn⁹⁴ is located within the third complementarity-determining region (CDR). Due to the structurally disruptive conditions used to prepare the peptide mapping samples, it cannot be ruled out that the deamidation observed at Asn⁹⁴ may have been generated during the tryptic digestion procedure. No deamidation was observed at any other asparagine residue to any detectable level. The result suggests that deamidation of asparagine is not expected to occur to any appreciable level during the manufacture of H1H685P.

The potential for oxidation of surface methionine residues, which can potentially affect H1H685P stability and activity, was also examined. H1H685P contains three methionine residues located within the heavy chain. Some of the methionine residues are predicted to be located on the surface of the antibody making them susceptible for oxidation. Oxidation of the methionine side chain to the sulfide form increases the side chain mass by 16 daltons, and makes the side chain more polar. Extensive mass data analysis, focused on the methionine-containing peptides, revealed no oxidation at any of the three methionine residues in any of the tested lots of H1H685P, suggesting that expression and purification processes as well as storage conditions of the drug substances does not result in chemical changes to the protein.

Example 12

Glycosylation Patterns

Glycosylation is a major post-translational modification that can lead to molecular mass heterogeneity of antibodies. Human IgG1 isotype antibodies contain a single canonical asparagine-linked (N-linked) glycosylation site located within the heavy chain constant region (Fc domain). Analysis of the reduced H1H685P tryptic map identified two glycopeptides corresponding to two tryptic peptides from the Fc domain (amino acid sequences of ²⁹⁸EEQFNSTYR³⁰⁶ (SEQ ID NO: 534) and ²⁹⁴TKPREEQFNSTYR³⁰⁶ (SEQ ID NO: 535)). The major glycan forms on these glycopeptides were elucidated based on MS analysis, and are summarized in Table 8. Glycopeptide mass analysis revealed that the H1H685P N-linked sugar is predominantly composed of a complex, bi-antennary structure, with a core fucose and zero, one, or two galactose residues at the glycan chain termini. These structures are consistent with the typical glycan forms found on recombinant antibodies expressed from mammalian cells. The LC/MS analysis also revealed a peptide containing the Fc glycosylation site (Asn³⁰²) but lacking glycan occupancy (peak 18 and peak 23). Integration of the peak areas in the UV chromatograms showed the 4.8% and 5.2% of N-linked sites at the Fc exhibited no glycan occupancy in the toxicology and clinical lots, respectively. These results are in agreement with the capillary electrophoresis analysis. The MS analysis of each of the peptides generated from the tryptic map reveals that H1H685P has no other N-linked or O linked glycosylation sites within the H1H685P antibody molecule.

TABLE 8

Peak No. ^a	Retention Time (min) ^b	Fragment Identity ^c	Observed	Expected	Comments
			Peptide Mass ^d (Da)	Peptide Mass ^e (Da)	
1	8.8	H220-223	471.294	471.269	
2	9.0	H340-343	447.287	447.269	
3	9.9	H326-331	734.390	734.374	
4	11.3	H219-223	599.390	599.364	
5	11.9	L184-188	624.303	624.275	
6	12.9	L184-190	889.461	889.429	
7	15.1	L208-211	522.279	522.255	
8	15.3	H361-365	604.334	604.306	
9	17.2	H216-223	941.611	941.554	
10	18.0	L19-24	706.372	706.343	
11	18.5	L208-214	868.376	868.349	
12	19.2	L104-107	487.331	487.300	
13	20.3	H415-421	817.490	817.465	
14	20.4	H415-419	574.348	574.332	
15	20.6	L104-108	643.428	643.401	
16	21.0	H298-306	2957.177	2957.144 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂ (Gal) ₂	
		H298-306	2795.150	2795.091 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂ (Gal)	
		H298-306	2592.198	2592.011 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₁ (Gal) ₁	
		H298-306	2429.972	2429.959 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc)	
		H298-306	2405.031	2404.927 (GlcNAc) ₂ (Man) ₅	
17	21.1	H298-306	2633.086	2633.038 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂	
		H298-306	2487.066	2486.980 (GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂	
		H298-306	2283.996	2283.901 (GlcNAc) ₂ (Man) ₃ (GlcNAc)	
		H298-306	2267.995	2267.917 Fuc(GlcNAc) ₂ (Man) ₂ (GlcNAc)	
		H298-306	2226.959	2226.879 Fuc(GlcNAc) ₂ (Man) ₃	
		H298-306	2121.904	2121.848 (GlcNAc) ₂ (Man) ₂ (GlcNAc)	
		H298-306	2080.957	2080.821 (GlcNAc) ₂ (Man) ₃	
18	22.0	H298-306	1188.547	1188.505 non-glycosylated	
19	22.6	L56-62	728.413	728.381	
20	23.0	H294-306	3277.467	3277.387 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂ (Gal) ₁	
		H294-306	3439.492	3439.440 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂ (Gal) ₂	
21	23.1	H294-306	3115.411	3115.335 Fuc(GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂	
		H294-306	2969.325	2969.277 (GlcNAc) ₂ (Man) ₃ (GlcNAc) ₂	
		H294-306	2766.276	2766.198 (GlcNAc) ₂ (Man) ₃ (GlcNAc) ₁	
22	23.8	L146-149	559.340	559.311	
23	24.2	H294-306	1670.876	1670.801 non-glycosylated	
24	27.9	L150-169	2135.024	2134.961	
25	28.8	H67-75	1064.579	1064.561	
26	29.5	H87-97	1245.589	1245.544	
27	29.9	H65-75	1277.733	1277.683	
28	30.6	H65-71	835.491	835.466	
29	30.9	H445-452	787.493	787.443 Heavy Chain with C-terminal K (1.5%)	
30	32.8	H445-451	659.364	659.349 Heavy Chain C-terminal K Removal (=98.5%)	
31	33.2	H254-260	834.459	834.426	
		H332-339	837.515	837.495	
32	35.9	L189-207	2140.139	2140.073	
33	37.0	L191-207	1874.980	1874.919	
34	37.4	L184-207	2746.385	2746.338	
35	38.0	L47-55	978.584	978.549	
36	40.6	H344-365	2509.374	2509.328	
		L146-169	2676.313	2676.262	
37	41.1	H350-365	1872.004	1871.962	
		H139-152	1320.696	1320.670	
38	44.6	H366-375	1160.680	1160.622	
		H127-138	1185.692	1185.639	
39	45.8	L170-183	1501.801	1501.750	
40	46.3	L63-78	1631.823	1631.778	
		L25-46	2452.250	2452.213	
		H1-19	1881.052	1880.995	
41	47.2	H76-86	1337.715	1337.675	
42	47.9	L150-183	3618.780	3618.701	
		H280-293	1676.822	1676.794	
43	48.5	L1-18	1883.018	1882.999	
44	48.9	H261-279	2138.056	2138.019	
45	49.8	H420-444	3043.452	3043.392	
46	50.1	H422-444	2800.328	2800.259	
47	51.0	L56-78	2342.233	2342.150	
48	51.9	L79-103	2997.316	2997.300 N ₉₄ S partial deamidation (4.2%)	
49	52.3	L79-103	2996.373	2996.292	
50	52.7	L146-183	4160.162	4161.003	
51	53.0	L79-108	3621.812	3621.683	

TABLE 8-continued

Peptide Assignments From Tryptic Map						
Peak No. ^a	Retention Time (min) ^b	Fragment Identity ^c	Observed Peptide Mass ^d (Da)	Expected Peptide Mass ^e (Da)	Comments	
52	53.4	H376-397	2544.165	2544.131	N ₃₈₉ G partial deamidation	
53	53.7	H376-397	2543.220	2543.123		
54	54.6	H39-64	2651.450	2651.322		
55	55.0	H350-375	3014.715	3014.574		
56	56.3	H398-414	1872.973	1872.914		
		H44-66	2166.157	2166.063		
57	57.7	H20-38	2203.060	2203.015		
58	58.5	L109-126	1945.065	1945.019		
59	61.5	H224-253	3333.696	3333.634		
60	62.8	H228-253	2843.510	2843.450		
61	63.6	H307-325	2227.254	2227.199		
62	64.2	L127-142	1796.938	1796.887		
63	65.3	H307-322	1807.042	1806.999		
64	65.7	H228-260	3659.800	3659.866		
65	66.4	H376-414	4398.082	4398.027		
66	69.5	L150-183	3618.780	3618.701		
67	73.1	H153-223	7635.962	7635.851		
68	73.5	H153-219	7182.596	7182.592		
69	74.0	H153-218	7054.603	7054.497		
70	74.4	H153-215	6712.410	6712.307		
71	76.4	H139-223	8938.581	8938.511		
72	76.8	H139-219	8485.280	8485.252		
73	77.3	H139-218	8357.136	8357.157		
74	77.6	H139-215	8014.698	8014.967		
75	78.9	H98-126	1985.620	2985.548		

^aColumn 1: Peak numbers corresponding to the chromatographic peak numbers.^bColumn 2: Retention time of each peptide peak in minutes.^cColumn 3: Location of peptide within the H1H685P sequences. H and L denote sequences located within H1H685P heavy chain and light chain, respectively.^dColumn 4: Experimentally determined peptide mass from LC/MS and LC/MS/MS analysis.^eColumn 5: Theoretical peptide mass calculated from predicted trypsin digestion cleavage sites within the amino acid sequence of H1H685P sequence.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 535

<210> SEQ ID NO 1
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 1

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tcc tctgtcgac cctctggatt cacctt cagt agt acgaca tacactgggt ccgtcaagct 120
acaggaaaag gtctggatgt ggtctca gat attggtcctg ctggta gac acatactatcca 180
ggctccgtga agggeccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
caa atgaaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag aggtttgatt 300
acgtttgggg ggcttatcgc cccg tttgac tactggggcc agggaaacctt ggtcaccgtc 360
tcctca 366
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<210> SEQ ID NO 2
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 2

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Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Asp Ile His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Ala Ile Gly Pro Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
 50 55 60
 Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
 65 70 75 80
 Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95
 Arg Gly Leu Ile Thr Phe Gly Gly Leu Ile Ala Pro Phe Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 3
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 3

ggattcacct tcagtagcta cgac

24

<210> SEQ ID NO 4
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 4

Gly Phe Thr Phe Ser Ser Tyr Asp
 1 5

<210> SEQ ID NO 5
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 5

attggtcctg ctggtgacac a

21

<210> SEQ ID NO 6
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 6

Ile Gly Pro Ala Gly Asp Thr
 1 5

<210> SEQ ID NO 7
<211> LENGTH: 48
<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 7

gcaagagggt tgattacgtt tggggggctt atcgccccgt ttgactac 48

<210> SEQ ID NO 8
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 8

Ala Arg Gly Leu Ile Thr Phe Gly Gly Leu Ile Ala Pro Phe Asp Tyr			
1	5	10	15

<210> SEQ ID NO 9
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 9

gacatccagt tgacccagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc	60
ctctcctgca gggccagtca gagtgtagc agcacctact tagcctggta ccagcagaaa	120
cctggccagg ctcccaggct cctcatctat ggtgcatacca gcagggccac tggcatccca	180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag	240
cctgaagatt ttgcagtgtt ttactgtcag cattatgata actcacaaac gttcggccaa	300
gggaccaagg tggaaatcaa acga	324

<210> SEQ ID NO 10
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 10

Asp Ile Gln Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly			
1	5	10	15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Thr		
20	25	30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu		
35	40	45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser		
50	55	60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Asp Asn Ser Gln		
85	90	95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg	
100	105

<210> SEQ ID NO 11
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 11

cagagtgtta gcagcaccta c

21

<210> SEQ ID NO 12
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 12

Gln Ser Val Ser Ser Thr Tyr
 1 5

<210> SEQ ID NO 13
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 13

ggtgtcatcc

9

<210> SEQ ID NO 14
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 14

Gly Ala Ser
 1

<210> SEQ ID NO 15
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 15

cagcattatg ataactcaca aacg

24

<210> SEQ ID NO 16
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 16

Gln His Tyr Asp Asn Ser Gln Thr
 1 5

<210> SEQ ID NO 17
 <211> LENGTH: 366
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 17

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gagggtgcagc tggggagtc tggggaggc ttgggtacagc cgggggggtc cctgagactc	60
tccctgtcgac cctctggatt cacccatcgat agctacgaca tacactgggt ccgtcaagct	120
acaggaaaag gtctggagt ggtctcgat attgggtcctg ctggtgacac atactatcca	180
ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt	240
caaataaca gcctgagagc cggggacacg gctgtgtatt actgtgcaag aggtttgatt	300
acgtttgggg ggcttatcgc cccgttgac tactggggcc agggaaacctt ggtcaccgtc	360
tcctca	366

<210> SEQ ID NO 18

<211> LENGTH: 122

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 18

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly			
1	5	10	15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
20	25	30	

Asp Ile His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu Glu Trp Val			
35	40	45	

Ser Ala Ile Gly Pro Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys			
50	55	60	

Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu			
65	70	75	80

Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala			
85	90	95	

Arg Gly Leu Ile Thr Phe Gly Gly Leu Ile Ala Pro Phe Asp Tyr Trp			
100	105	110	

Gly Gln Gly Thr Leu Val Thr Val Ser Ser		
115	120	

<210> SEQ ID NO 19

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 19

gaaaatttgt tgacgcagtc tccaggcacc ctgtctttgt ctccaggggaa aagagccacc	60
ctctccgtca gggccagtc gagtgtagc agcacctact tagcctggta ccagcagaaa	120
cctggccagg ctccccaggct cctcatctat ggtgcattca gcagggccac tggcatccca	180
gacaggttca gtggcagtggt gtcctggaca gacttcactc tcaccatcag cagactggag	240
cctgaagatt ttgcgtgtt ttactgtcag cattatgata actcacaaac gttcggccaa	300
gggaccaagg tggaaatcaa a	321

<210> SEQ ID NO 20

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

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45**46**

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<400> SEQUENCE: 20

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1															
							10								15

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Thr
				20			25								30

Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
					35		40								45

Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
				50		55									60

Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
					65		70		75						80

Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Tyr	Asp	Asn	Ser	Gln
					85		90								95

Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys					
					100		105								

<210> SEQ ID NO 21

<211> LENGTH: 366

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 21

gaggtgcagc	tggtgaggc	tgggggaggc	ttggtagacgc	ctggggggtc	cctgagactc	60
------------	-----------	------------	-------------	------------	------------	----

tcctgtcgac	cctctggatt	caccttcagt	agctacgaca	tgcactgggt	ccgccaagct	120
------------	------------	------------	------------	------------	------------	-----

acaggaaaag	gtctggagtg	ggtctcagct	attggctctg	ctggtgacac	atactatcca	180
------------	------------	------------	------------	------------	------------	-----

ggctccgtga	agggccgatt	caccatctcc	agagaaaatg	ccaagaactc	cttgtatctt	240
------------	------------	------------	------------	------------	------------	-----

caaataaca	gcctgagage	cggggacacg	gctgtgtatt	actgtgcaag	aggtttgatt	300
-----------	------------	------------	------------	------------	------------	-----

acgtttgggg	ggcttatcgc	cccggttgc	tactggggcc	agggAACCT	ggtcaccgtc	360
------------	------------	-----------	------------	-----------	------------	-----

tcctca						366
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<210> SEQ ID NO 22

<211> LENGTH: 122

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 22

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Ley	Val	Gln	Pro	Gly	Gly
1														
					5		10							15

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
				20			25								30

Asp	Met	His	Trp	Val	Arg	Gln	Ala	Thr	Gly	Lys	Gly	Ley	Glu	Trp	Val
					35		40								45

Ser	Ala	Ile	Gly	Pro	Ala	Gly	Asp	Thr	Tyr	Tyr	Pro	Gly	Ser	Val	Lys
					50		55								60

Gly	Arg	Phe	Thr	Ile	Ser	Arg	Glu	Asn	Ala	Lys	Asn	Ser	Leu	Tyr	Leu
					65		70		75						80

Gln	Met	Asn	Ser	Leu	Arg	Ala	Gly	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala
					85		90								95

Arg	Gly	Leu	Ile	Thr	Phe	Gly	Ley	Ile	Ala	Pro	Phe	Asp	Tyr	Trp	
					100		105								110

Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser						
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115

120

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<210> SEQ ID NO 23
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 23

gaaattgtgt tgacgcagtc tccaggcacc ctgtcttgc ctccagggga aagagccacc      60
ctctcctgc gggccagtca gagtgtagc agcacctact tagcctggta ccagcagaaa      120
cctggccagg cttccaggct cctcatctat ggtgcatacca gcagggccac tggcatccca      180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag      240
cctgaagatt ttgcagtgtt ttactgtcag cattatgata actcacaaac gttcgccaa      300
gggaccaagg tggaaatcaa ac                                         322

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<210> SEQ ID NO 24
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 24

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1           5          10          15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Thr
20          25          30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35          40          45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50          55          60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65          70          75          80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Asp Asn Ser Gln
85          90          95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100         105

```

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<210> SEQ ID NO 25
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 25

gaggtgcagc tggcagtc tgggggaggc ttgggtcagc ctggggagtc cctgagactc      60
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccggcagggt      120
ccagggaaagg gcctggagt ggtctcaagt attactggga gtggtgatac cacataactac      180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcacatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattt      300
cttgactaca gtacctaccc tggctttgtt ctctggggcc aaggaaat ggtcaccgtc      360
tcttca                                         366

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<210> SEQ ID NO 26
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 26

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Glu
1           5          10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20          25          30

Ala Met Ser Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
35          40          45

Ser Ser Ile Thr Gly Ser Gly Asp Thr Thr Tyr Tyr Ala Asp Ser Val
50          55          60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70          75          80

Leu His Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu Trp
100         105         110

Gly Gln Gly Thr Met Val Thr Val Ser Ser
115         120

```

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<210> SEQ ID NO 27
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 27

ggattcacct ttagcagcta tgcc

24

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<210> SEQ ID NO 28
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 28

```

Gly Phe Thr Phe Ser Ser Tyr Ala
1           5

```

```

<210> SEQ ID NO 29
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 29

attactggga gtgggtatac caca

24

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<210> SEQ ID NO 30
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 30

Ile Thr Gly Ser Gly Asp Thr Thr
1 5<210> SEQ ID NO 31
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 31

gcgaaagatt ttcttgacta cagtagttac ctgtgttttg atctc 45

<210> SEQ ID NO 32
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 32

Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu
1 5 10 15<210> SEQ ID NO 33
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 33

gacatccaga tgaccaggc tccagccacc ctgtctttgt ctccaggggaa aagagccacc 60
ctctccgtca gggccaggta gagtgtttgc agctacttaa cctggcacca gcagaaacct 120
ggccaggctc ccaggctcct cagctatgtat gcatctaaca gggccactgg catcccagcc 180
aggttcagtgc cagtggttc tgggacagac ttcactctca ccatcagcag cctagagcct 240
gaagattttgc cagtttataa ctgtcagcag ctagcaact ggccgcctcac tttcgccgga 300
ggaccaagg tggaaatcaa acga 324<210> SEQ ID NO 34
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 34

Asp Ile Gln Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ser
35 40 45Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu
85 90 95

-continued

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> SEQ ID NO 35
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 35

cagagtgtta gcagctac

18

<210> SEQ ID NO 36
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 36

Gln Ser Val Ser Ser Tyr
1 5

<210> SEQ ID NO 37
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 37

gatgcattc

9

<210> SEQ ID NO 38
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 38

Asp Ala Ser
1

<210> SEQ ID NO 39
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 39

cagcagcgta gcaactggcc gctcact

27

<210> SEQ ID NO 40
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 40

Gln Gln Arg Ser Asn Trp Pro Leu Thr
1 5

-continued

<210> SEQ ID NO 41
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 41

gagggtgcagc	tgggtggagtc	tgggggaggc	ttgggttcagc	ctggggagtc	cctgagactc	60
tcctgtgcag	cctctggatt	cacctttagc	agctatgcca	tgagctgggt	ccgccagggt	120
ccagggaaagg	gcctggagtg	ggtctcaagt	attactggga	gtggtgatac	cacataactac	180
gcagactccg	tgaaggggccg	gttcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcacatga	acagcctgag	agccgaggac	acggccgtat	attactgtgc	gaaagattt	300
cttgactaca	gtacctacct	tgctttgtat	ctctggggcc	aagggacaat	ggtcaccgtc	360
tcttca						366

<210> SEQ ID NO 42
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 42

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Glu
1					5			10				15			
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
					20			25			30				
Ala	Met	Ser	Trp	Val	Arg	Gln	Gly	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
					35			40			45				
Ser	Ser	Ile	Thr	Gly	Ser	Gly	Asp	Thr	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
		50			55			60							
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
		65			70			75			80				
Leu	His	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90			95				
Ala	Lys	Asp	Phe	Leu	Asp	Tyr	Ser	Thr	Tyr	Leu	Ala	Phe	Asp	Leu	Trp
					100			105			110				
Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser						
					115			120							

<210> SEQ ID NO 43
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 43

gaaaatttgt	tgacacagtc	tccagccacc	ctgtctttgt	ctccaggggta	aagagccacc	60
ctctcctgca	gggccagtca	gagtgttagc	agctacttaa	cctggtagcca	gcagaaacct	120
ggccaggctc	ccaggctcct	cagctatgtat	gcatctaaca	gggccactgg	catcccagcc	180
aggttcagtg	gcagtggttc	tgggacagac	ttcactctca	ccatcagcag	cctagagcct	240
gaagattttg	cagtttatta	ctgtcagcag	cgtagcaact	ggccgctcac	tttcggcgga	300
gggaccaagg	tggagatcaa	a				321

-continued

<210> SEQ ID NO 44
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 44

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1															
															15
Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr
															30
Leu	Thr	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ser
															45
Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
															60
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro
															80
Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Arg	Ser	Asn	Trp	Pro	Leu
															95
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys					
															105

<210> SEQ ID NO 45
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 45

gagggtgcagc	tggtgagtc	tggggaggc	tgggtacagc	ctgggggtc	cctgagactc	60
tcctgtgcag	cctctggatt	cacctttagc	agctatgcc	tgagctgggt	ccgcccaggct	120
ccagggaaagg	ggctggagt	ggtctcagct	attactggga	gtggtgatac	cacataactac	180
gcagactccg	tgaagggccc	gttccaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggccgtat	attactgtgc	gaaagat	300
cttgactaca	gtacctacct	tgctttgtat	ctctggggcc	aagggacaat	ggtcaccgtc	360
tcttca						366

<210> SEQ ID NO 46
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 46

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1															
															15
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
															30
Ala	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
															45
Ser	Ala	Ile	Thr	Gly	Ser	Gly	Asp	Thr	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
															60
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr

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65	70	75	80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu Trp			
100	105	110	
Gly Gln Gly Thr Met Val Thr Val Ser Ser			
115	120		

<210> SEQ ID NO 47
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 47

gaaattgtgt tgacacagtc tccagccacc ctgtctttgt ctccaggggaa aagagccacc	60
ctctcctgca gggccagtca gagtgtagc agtactatcg cctggtagcca acagaaacct	120
ggccagggttc ccagggtctt catctatgtat gcatctaaca gggccactgg catcccagcc	180
aggttcagtg gcagtggttc tgggagagac ttcaactctca ccatcagcag cctagagcct	240
gaagattttg cagtttatta ctgtcagcag cgtagcaact ggccgtcac tttcggcgga	300
gggaccaagg tggagatcaa ac	322

<210> SEQ ID NO 48
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 48

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly	
1 5 10 15	
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr	
20 25 30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile	
35 40 45	
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly	
50 55 60	
Ser Gly Ser Gly Arg Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro	
65 70 75 80	
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Leu	
85 90 95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys	
100 105	

<210> SEQ ID NO 49
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 49

caggtgcagc tgggtggagtc tgggggaggc ttgggtgcagc ctggcagggtc cctgagactc	60
tcctgtgcag cctctggatt cacctttgat gattatgccca tgcactgggt ccggcaagct	120
ccagggaaagg gcctggagtg ggtctcaggat attagttgaa atagttgtga cataggctat	180

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gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat	240
ctgcaaatga acagtctgag agctcaggac acggccttgc attactgtgc aaaagcttac	300
ggtgactact actacttta cggtatggac gtctggggcc aagggaccac ggtcacccgc	360
tcctca	366

<210> SEQ ID NO 50
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 50

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg	
1 5 10 15	
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr	
20 25 30	
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
35 40 45	
Ser Gly Ile Ser Trp Asn Ser Gly Asp Ile Gly Tyr Ala Asp Ser Val	
50 55 60	
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr	
65 70 75 80	
Leu Gln Met Asn Ser Leu Arg Ala Gln Asp Thr Ala Leu Tyr Tyr Cys	
85 90 95	
Ala Lys Ala Tyr Gly Asp Tyr Tyr Phe Tyr Gly Met Asp Val Trp	
100 105 110	
Gly Gln Gly Thr Thr Val Thr Val Ser Ser	
115 120	

<210> SEQ ID NO 51
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 51

ggattcacct ttgatgatta tgcc	24
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<210> SEQ ID NO 52
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 52

Gly Phe Thr Phe Asp Asp Tyr Ala	
1 5	

<210> SEQ ID NO 53
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 53

attagttgga atagtggta cata	24
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<210> SEQ_ID NO 54
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 54

Ile Ser Trp Asn Ser Gly Asp Ile
1 5

<210> SEQ_ID NO 55
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 55

gcaaaaagctt acgggtgacta ctactacttt tacggtatgg acgtc 45

<210> SEQ_ID NO 56
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 56

Ala Lys Ala Tyr Gly Asp Tyr Tyr Tyr Phe Tyr Gly Met Asp Val
1 5 10 15

<210> SEQ_ID NO 57
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 57

gacategtga tgacccagtgc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctccctgca gggccagtc gagggttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctccttcgtt agtgcattca gcagggccac tggcatccca 180
gacaggttca gtggcagtgg gtcctggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagtgtt ttactgttag cagtatgata actcactcac tttcgccgga 300
gggaccaaag tggatatcaa acga 324

<210> SEQ_ID NO 58
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 58

Asp Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

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Ile Phe Ser Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Ser Leu
 85 90 95

Thr Phe Gly Gly Thr Lys Val Asp Ile Lys Arg
 100 105

<210> SEQ ID NO 59
 <211> LENGTH: 21
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 59

cagagtgtta gcagcagctt c

21

<210> SEQ ID NO 60
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 60

Gln Ser Val Ser Ser Ser Tyr
 1 5

<210> SEQ ID NO 61
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 61

agtgcattcc

9

<210> SEQ ID NO 62
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 62

Ser Ala Ser
 1

<210> SEQ ID NO 63
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 63

cagcagtagtataactcact cact

24

<210> SEQ ID NO 64
 <211> LENGTH: 8
 <212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 64

Gln Gln Tyr Asp Asn Ser Leu Thr
 1 5

<210> SEQ ID NO 65
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 65

gaagtgcagc	tgggtggagtc	tgggggaggc	ttgggtgcagc	ctggcaggc	cctgagactc	60
tccctgtgcag	cctctggatt	cacctttgtat	gattatgccca	tgcactgggt	ccggcaagct	120
ccagggaaagg	gcctggagtg	ggtctcaggat	attagttggaa	atagtggta	cataggctat	180
ggggactctg	tgaagggccg	attcaccatc	tccagagaca	acgccaagaa	ctccctgtat	240
ctgcaaatga	acagtctgag	agctcaggac	acggccttgt	attactgtgc	aaaagcttac	300
ggtgactact	actactttta	cggttatggac	gtctggggcc	aagggaccac	ggtcaccgtc	360
tcc						363

<210> SEQ ID NO 66
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 66

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Asp Ile Gly Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Gln Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Ala Lys Ala Tyr Gly Asp Tyr Tyr Phe Tyr Gly Met Asp Val Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser
 115 120

<210> SEQ ID NO 67
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 67

gaaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggaa aagagccacc 60

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ctctcctgca gggccagtca gagtgtagc agcagctact tagcctggta ccagcagaaa	120
cctggccagg ctcccaggct cctcatctt agtgcaccca gcagggccac tggcatccca	180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag	240
cctgaagatt ttgcagtgtt ttactgtcag cagtatgata actcaactcac tttcggcgga	300
gggaccaagg tggagatcaa a	321

<210> SEQ ID NO 68
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 68

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly			
1	5	10	15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser			
20	25	30	
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu			
35	40	45	
Ile Phe Ser Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser			
50	55	60	
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Ser Leu			
85	90	95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 69
<211> LENGTH: 364
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 69

gaagtgcagc tggggaggc ttgggtacagc ctggcaggc cctgagactc	60
tcctgtgcag cctctggatt caccttgcatt gattatgcac tgcactgggt ccggcaagct	120
ccagggaaagg gcctggaggc ggtctcaggc attagttggaa atagttgtgc cataggctat	180
gcggactctg tgaaggggccg attcaccatc tccagagaca acgccaagaa ctccctgtat	240
ctgcaaatga acagtctgag agctgaggac acggccttgtt attactgtgc aaaagcttac	300
ggtgactact actacttttgc cggatggac gtctggggcc aagggaccac ggtcaccgtc	360
tcct	364

<210> SEQ ID NO 70
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 70

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Arg			
1	5	10	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr			

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20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Asp Ile Gly Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Ala Lys Ala Tyr Gly Asp Tyr Tyr Phe Tyr Gly Met Asp Val Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser
 115 120

<210> SEQ ID NO 71

<211> LENGTH: 322

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 71

gaaaattgtgt	tgacgcagtc	tccaggcacc	ctgtctttgt	ctccagggga	aagagccacc	60
ctctcctgca	gggccagtca	gagtggttagc	agcagctact	tagcctggta	ccagcagaaaa	120
cctggccagg	ctcccccaggct	cctcatctat	agtgcatacca	gcagggccac	tggcatccca	180
gacaggttca	gtggcagtgg	gtctggaca	gacttcactc	tcaccatcag	cagactggag	240
cctgaagatt	ttgcagtgt	taactgtcag	cagtatgata	actcaactcac	tttcggcgga	300
gggaccaagg	tggagatcaa	ac				322

<210> SEQ ID NO 72

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 72

Glu Ile Val Leu Thr Gln Ser Pro Gly	Thr Leu Ser Leu Ser Pro Gly		
1	5	10	15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser		
20	25	30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu		
35	40	45

Ile Tyr Ser Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser		
50	55	60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asp Asn Ser Leu		
85	90	95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys		
100	105	

<210> SEQ ID NO 73

<211> LENGTH: 366

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 73

caggtgcagc tggggaggc ttgggttcagc ctggggaggc cctgagactc	60
tccctgtcgac cctctggatt cacctttagc agctatgccca tgagctgggt ccggccagggt	120
ccagggaaagg gcctggaggc ggtctcaagt attagtggga gtgggtggtac cacttactac	180
gcagactccg tggaggggccg gttcaccatc tccagagaca attccaagaa cacgtgttat	240
ctgcacatga acagecctgag agccgaggac acggccgtat attactgtgc gaaagat	300
cttgactaca gtacaccttgc tgcttttgc ctctggggcc aagggacaat ggtcaccgtc	360
tcttca	366

<210> SEQ ID NO 74

<211> LENGTH: 122

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 74

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Glu			
1	5	10	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
20	25	30	
Ala Met Ser Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val			
35	40	45	
Ser Ser Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val			
50	55	60	
Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
65	70	75	80
Leu His Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu Trp			
100	105	110	
Gly Gln Gly Thr Met Val Thr Val Ser Ser			
115	120		

<210> SEQ ID NO 75

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 75

ggattcacct ttagcagcta tgcc 24

<210> SEQ ID NO 76

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 76

Gly Phe Thr Phe Ser Ser Tyr Ala	
1	5

<210> SEQ ID NO 77

-continued

<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 77

attagtgggta cact

24

<210> SEQ ID NO 78
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 78

Ile Ser Gly Ser Gly Gly Thr Thr
1 5

<210> SEQ ID NO 79
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 79

gcgaaaagatt ttcttgacta cagtagttac cttgttttg atctc

45

<210> SEQ ID NO 80
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 80

Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu
1 5 10 15

<210> SEQ ID NO 81
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 81

gacatccaga tgaccaggc	tccatcttcc gtgtctgcat ctgttaggaga cagagtacc	60
atcaacttgc gggcgagtca	gggtttagc agctggtag cctggatca gcagaaacca	120
ggaaaagccc otaagctcct	gatctatgct gcatccagg tgcggatgg ggtccatca	180
aggttcagcg gcagtggtac	tgggacat ttcactctca ccatcagcag cctgcagcct	240
gaagattttg caacttacta	ttgtcaacag gctaacagt tccctggac gttcggcaa	300
gggaccaagg tggagatcaa acga		324

<210> SEQ ID NO 82
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 82

-continued

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Ile
 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Arg
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 100 105

<210> SEQ ID NO 83
 <211> LENGTH: 18
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 83

cagggatttttgcagctgg

18

<210> SEQ ID NO 84
 <211> LENGTH: 6
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 84

Gln Gly Ile Ser Ser Trp
 1 5

<210> SEQ ID NO 85
 <211> LENGTH: 9
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 85

gctgcatcc

9

<210> SEQ ID NO 86
 <211> LENGTH: 3
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 86

Ala Ala Ser
 1

<210> SEQ ID NO 87
 <211> LENGTH: 27
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 87

caacaggcta acagttccc tcggacg

27

<210> SEQ ID NO 88

<211> LENGTH: 9

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 88

Gln Gln Ala Asn Ser Phe Pro Arg Thr
1 5

<210> SEQ ID NO 89

<211> LENGTH: 366

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 89

gaggtgcagc tgggggagtc tgggggaggc ttgggtttagc ctggggagtc cctgagactc	60
tccctgtgcag cctctggatt caccttttagc agctatgccca tgagctgggt ccggccagggt	120
ccagggaaagg gcctggagtg ggtctcaagt attagtgggg gtgggtggtac cacttactac	180
gcagactccg tggaggggccg gttcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcacatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagattt	300
cttgactaca gtacctacct tgctttttagt ctctggggcc aagggacaat ggtcacccgtc	360
tcttca	366

<210> SEQ ID NO 90

<211> LENGTH: 122

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 90

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Glu
1 5 10 15Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30Ala Met Ser Trp Val Arg Gln Gly Pro Gly Lys Gly Leu Glu Trp Val
35 40 45Ser Ser Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80Leu His Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95Ala Lys Asp Phe Leu Asp Tyr Ser Thr Tyr Leu Ala Phe Asp Leu Trp
100 105 110Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120<210> SEQ ID NO 91
<211> LENGTH: 321

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 91

```

gacatccaga tgacctagtc tccatcttcc gtgtctgcat ctgttaggaga cagagtcacc      60
atcacttgtc gggcgagtca gggatttagc agctggtag cctggtatca gcagaaacca      120
gggaaagccc ctaagctcct gatctatgtc gcatccagg tgcggaaatgg ggtcccatca      180
aggttcagcg gcagtggtatc tgggacatgt ttcacttca ccatcagcag cctgcaggct      240
gaagattttgc aacttacta ttgtcaacag gctaacagtt tccctcgac gttcgccaa      300
gggaccaagg tggaaatcaa a                                              321

```

<210> SEQ ID NO 92
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 92

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1          5           10          15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
20         25           30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35         40           45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50         55           60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65         70           75           80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Arg
85         90           95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100        105

```

<210> SEQ ID NO 93
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 93

```

gaggtgcagc tgggtggagtc tgggggaggc ttggtagc ctggggggtc cctgagactc      60
tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccggcaggct      120
ccagggaaagg ggctggagtg ggtctcagct attagtggaa gtgggtgtac cacttactac      180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcaaatacgtc acagcctgag agccgaggac acggccgtat attactgtgc gaaagattt      300
cttgactaca gtacctacatc tgctttgtat ctctggggcc aagggacaat ggtcaccgtc      360
tcttca                                              366

```

<210> SEQ ID NO 94
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 94

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1							5		10				15		

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
	20						25					30			

Ala	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35						40				45				

Ser	Ala	Ile	Ser	Gly	Ser	Gly	Gly	Thr	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
	50						55			60					

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65					70				75			80			

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
		85				90					95				

Ala	Lys	Asp	Phe	Leu	Asp	Tyr	Ser	Thr	Tyr	Leu	Ala	Phe	Asp	Leu	Trp
		100				105				110					

Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser						
	115						120								

<210> SEQ ID NO 95

<211> LENGTH: 322

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 95

gacatccaga	tgaccaggc	tccatcttct	gtgtctgcat	ctgttaggaga	cagagtccacc	60
atcacttgtc	gggcgagtca	gggttattagc	agctggtag	cctggtatca	gcagaaacca	120
ggaaaagccc	ctaagtcct	gatctatgt	gatccagg	tgc当地	ggtcccatca	180
aggttcagcg	gcagtggtatc	tggcacat	ttcactctca	ctatcagcag	cctgcagcct	240
gaagatTTG	caacttacta	ttgtcaacag	gctaacagtt	tccctggac	gttcggccaa	300
gggaccaagg	tggaaatcaa	ac				322

<210> SEQ ID NO 96

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 96

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Val	Ser	Ala	Ser	Val	Gly
1							5		10					15	

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Ser	Trp
	20					25						30			

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile
						35						40		45	

Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
		50				55					60				

Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
65					70				75			80			

Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ala	Asn	Ser	Phe	Pro	Arg
					85				90			95			

-continued

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 97
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 97

```
caggtgcagc tgggggaggc ttggtaaagc ctggggggtc ccttagactc      60
tccctgtcgac cctctggatt cactttcagt aacgcctgga tgagctgggt ccgccaggct    120
ccagggaaagg ggctggagtg ggttggccgt attaaaagca aaactgtatgg tgggacaaca    180
gactacgctg caccctgtgaa aggccagattc accatctcaa gagatgattc aaaaaacacg    240
ctgtatctgc aatgaacag cctgaaaacc gaggacacag ccgtgtattha ctgtaccaca    300
gatggcgttag cagctcgatc ctggactac tggggccagg gaaccttgtt caccgtctcc    360
tca                                         363
```

<210> SEQ ID NO 98
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 98

Gln Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
50 55 60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Thr Thr Asp Gly Val Ala Ala Arg Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 99
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 99

ggattcaacctt tcagtaaacgc ctgg 24

<210> SEQ ID NO 100
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 100

Gly	Phe	Thr	Phe	Ser	Asn	Ala	Trp
1							5

<210> SEQ ID NO 101

<211> LENGTH: 30

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 101

ataaaaagca aaactgatgg tgggacaaca

30

<210> SEQ ID NO 102

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 102

Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Thr
1								5	10

<210> SEQ ID NO 103

<211> LENGTH: 36

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 103

accacagatg gcgttagcagc tcgttacttt gactac

36

<210> SEQ ID NO 104

<211> LENGTH: 12

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 104

Thr	Thr	Asp	Gly	Val	Ala	Ala	Arg	Tyr	Phe	Asp	Tyr
1								5			10

<210> SEQ ID NO 105

<211> LENGTH: 324

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 105

gacatccaga tgacctagtc tccttccacc ctgtctgcat ctgttaggaga cagagtacc

60

atcaacttgcc gggccagtca gagtattagt agctgggtgg ctggtatca gcagaaacca

120

gggaaagccc ctaagctctt gatctataag gcgtctagtt tagaaagtgg ggtcccatca

180

aggttcagcg gcagtggtatc tgggacagaa ttcaactctca ccatcagcag cctgcagcct

240

gatgatTTTg caacttattt ctgccaacag tataatagtt attctcgac gttcggccaa

300

gggaccaagg tggagatcaa acga

324

-continued

<210> SEQ ID NO 106
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 106

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1															
															15

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Ser	Ser	Trp
															30
20															

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile
															45
35															

Tyr	Lys	Ala	Ser	Ser	Leu	Glu	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
															60
50															

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
															80
65															

Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Ser	Tyr	Ser	Arg
															95
85															

Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg				
															105
100															

<210> SEQ ID NO 107
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 107

cagagtattatgtatctgg															18
---------------------	--	--	--	--	--	--	--	--	--	--	--	--	--	--	----

<210> SEQ ID NO 108
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 108

Gln	Ser	Ile	Ser	Ser	Trp										
1															
															5

<210> SEQ ID NO 109
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 109

aaggcgtct															9
-----------	--	--	--	--	--	--	--	--	--	--	--	--	--	--	---

<210> SEQ ID NO 110
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 110

Lys Ala Ser

-continued

1

<210> SEQ ID NO 111
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 111

caacagtata atagttattc tcggacg

27

<210> SEQ ID NO 112
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 112

Gln Gln Tyr Asn Ser Tyr Ser Arg Thr
1 5

<210> SEQ ID NO 113
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 113

gagggtgcagc tggtgagtc tgggggaggc ttggtaaagc ctggggggtc ccttagactc	60
tccctgtcgac cctctggatt cactttcagt aacgcctgga tgagctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggttggccgt attaaaagca aaactgtatgg tgggacaaca	180
gactacgctg cacccgtgaa aggccgatcc accatctcaa gagatgatcc aaaaaacacg	240
ctgttatctgc aatgaacag cctgaaaacc gaggacacag ccgtgtatata ctgtaccaca	300
gatggcgttag cagctcgtaa ctttgactac tggggccagg gaaccctggt caccgtctcc	360
tca	363

<210> SEQ ID NO 114
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 114

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
50 55 60Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

-continued

Tyr Cys Thr Thr Asp Gly Val Ala Ala Arg Tyr Phe Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 115
 <211> LENGTH: 321
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 115

gacatccaga tgaccaggc	tccttccacc ctgtctgcat	ctgttaggaga cagagtacc	60
atcaacttgcc gggccaggta	gagttattgt agctggttgg	cctggtatca gcagaaacca	120
gggaaaagccc ctaagctcct	gatctataag gcgtctagtt	tagaaagtgg ggtcccatca	180
aggttcagcg gcagtggtac	tgggacagaa ttcactctca	ccatcagcag cctgcagcct	240
gatgattttg caacttatta	ctgccaacag tataatagtt	attctcggac gttcggccaa	300
gggaccaagg tggaaatcaa	a		321

<210> SEQ ID NO 116
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 116

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser Arg
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 117
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 117

gaggtgcagc tgggtggagtc	tgggggaggc ttggtaaagc	ctggggggtc ctttagactc	60
tcctgtgcag cctctggatt	cactttcagt aacgcctgga	tgagctgggt ccgccaggct	120
ccagggaaagg ggctggagtg	ggttggccgt attaaaagca	aaactgtatgg tgggacaaca	180
gactacgctg cacccgtgaa	aggcagattc accatctcaa	gagatgattc aaaaaacacg	240
ctgtatctgc aatgaacag	cctgaaaacc gaggacacag	ccgtgtatata ctgtaccaca	300

-continued

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 121

<211> LENGTH: 366

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 121

gagggtgcagc	tgggtgcagtc	tgggggaggc	gtgggtccagc	cggggaggc	cctgagactc	60
tccctgtcgac	cgtctggatt	cacccatcgat	agctatggca	tgcactgggt	ccggccaggct	120
ccaggcaagg	ggctggagtg	ggtggcagtt	atgtggatg	atgaaactaa	taaatactat	180
gcagactccg	tgaaggggccg	attaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggctgtgt	attactgtgc	gagatatagt	300
ggctacgagg	actactacca	cggttatggac	gtctggggcc	aagggaccac	ggtcaccgtc	360
tcctca						366

<210> SEQ ID NO 122

<211> LENGTH: 122

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 122

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Met Trp Tyr Asp Glu Thr Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Ser Gly Tyr Glu Asp Tyr Tyr His Gly Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 123

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 123

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ggattcacct tcagtagcta tggc 24

<210> SEQ ID NO 124
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 124

Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> SEQ ID NO 125
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 125

atgtggtatg atgaaaactaa taaa 24

<210> SEQ ID NO 126
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 126

Met Trp Tyr Asp Glu Thr Asn Lys
1 5

<210> SEQ ID NO 127
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 127

gcgagatata gtggctacga ggactactac cacggtatgg acgtc 45

<210> SEQ ID NO 128
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 128

Ala Arg Tyr Ser Gly Tyr Glu Asp Tyr Tyr His Gly Met Asp Val
1 5 10 15

<210> SEQ ID NO 129
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 129

gccccatccaga tgaccaggc tccagccacc ccgtctgtgt ctccaggggaa aagagccacc 60

ctctcctgca gggccagtca gagtattacg agcaacttag cctggtagcca gcagaaacct 120

-continued

```
ggccaggctc ccaggctct catctatggt gcatccacca gggccactgg tatcccagcc      180
aggttcagtgc cagtggggtc tgggacagag ttcaacttcac ccatcagcag cctgcagtct      240
gaagattttg cagtttatta ctgtcagcac tataataact ggatcacctt cggccaaggg      300
acacgactgg agatcaaacg a                                         321
```

<210> SEQ ID NO 130
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 130

Ala	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ala	Thr	Pro	Ser	Val	Ser	Pro	Gly
1								5		10				15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Ser	Ser	Asn
		20						25				30			

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
		35				40					45				

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
		50				55					60				

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
		65			70			75					80		

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Tyr	Asn	Asn	Trp	Ile	Thr
		85						90					95		

Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Arg					
		100					105								

<210> SEQ ID NO 131
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 131

```
cagagtatta gcagcaac                                         18
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<210> SEQ ID NO 132
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 132

```
Gln Ser Ile Ser Ser Asn
1           5
```

<210> SEQ ID NO 133
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 133

```
ggtgcatcc
```

<210> SEQ ID NO 134

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<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 134

Gly Ala Ser
1

<210> SEQ ID NO 135
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 135

cagcactata ataaactggat cacc 24

<210> SEQ ID NO 136
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 136

Gln His Tyr Asn Asn Trp Ile Thr
1 5

<210> SEQ ID NO 137
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 137

caggtgcagc tggtgaggc tgggggaggc gtggtccagc ctgggaggc cctgagactc	60
tccctgtcag cgtctggatt cacttcaagt agctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggagtg ggtggcagtt atgtggtagt atgaaaactaa taaatactat	180
gcagactccg tgaaggggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaaatga acagectgag agccgaggac acggctgtgt attactgtgc gagatatagt	300
ggctacgagg actactacca cggttatggac gtctggggcc aagggaccac ggtcaccgtc	360
tcc	363

<210> SEQ ID NO 138
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 138

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

-continued

Ala	Val	Met	Trp	Tyr	Asp	Glu	Thr	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
50						55			60						

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65					70				75		80				

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
						85		90			95				

Ala	Arg	Tyr	Ser	Gly	Tyr	Glu	Asp	Tyr	Tyr	His	Gly	Met	Asp	Val	Trp
						100		105		110					

Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser							
						115		120							

<210> SEQ ID NO 139

<211> LENGTH: 318

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 139

gaaaatagtga	tgacgcagtc	tccagccacc	ccgtctgtgt	ctccaggggaa	aagagccacc	60
ctctcctgca	gggccagtca	gagtagtttcg	agcaacttag	cctggtagcca	gcagaaacct	120
ggccaggctc	ccaggcttct	catctatggt	gcatccacca	gggccactgg	tatcccagcc	180
aggttcagtg	gcagtggttc	tgggacagag	ttcaactctca	ccatcagcag	cctgcagtc	240
gaagattttg	cagtttatta	ctgtcagcac	tataataact	ggatcacctt	cggccaaggg	300
acacgactgg	agattaaa					318

<210> SEQ ID NO 140

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 140

Glu	Ile	Val	Met	Thr	Gln	Ser	Pro	Ala	Thr	Pro	Ser	Val	Ser	Pro	Gly
1						5			10			15			

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Ser	Ser	Asn
				20					25			30			

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Ile	
						35		40			45				

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
						50		55			60				

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
						65		70		75			80		

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Tyr	Asn	Asn	Trp	Ile	Thr
						85		90		95					

Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys						
						100		105							

<210> SEQ ID NO 141

<211> LENGTH: 364

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 141

caggtgcagc tggggaggc gtgggtccagc ctggggaggc cctgagactc 60

tcctgtgcag cgtctggatt cacttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggagtg ggtggcagtt atgtggatg atgaaactaa taaatactat	180
gcagactccg tgaaggccc attcaccatc tccagagaca actccaagaa cacgctgtat	240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagatatagt	300
ggctacgagg actactacca cggtatggac gtctgggccc aagggaccac ggtcaccgtc	360
tcct	364

<210> SEQ ID NO 142
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 142

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg			
1	5	10	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
20	25	30	
Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
35	40	45	
Ala Val Met Trp Tyr Asp Glu Thr Asn Lys Tyr Tyr Ala Asp Ser Val			
50	55	60	
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
65	70	75	80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Arg Tyr Ser Gly Tyr Glu Asp Tyr Tyr His Gly Met Asp Val Trp			
100	105	110	
Gly Gln Gly Thr Thr Val Thr Val Ser			
115	120		

<210> SEQ ID NO 143
<211> LENGTH: 319
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 143

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc	60
ctctcctgca gggccagtca gagtattagc agcaacttag cctggatcca gcagaaacct	120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatccagcc	180
aggttcagtg gcagtggtc tggcacagag ttcaactctca ccatcagcag cctgcagtct	240
gaagattttg cagtttatta ctgtcagcac tataataact ggatcacctt cggccaaggg	300
acacgactgg agattaaac	319

<210> SEQ ID NO 144
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 144

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Glu	Ile	Val	Met	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
1					5				10				15		

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Ser	Ser	Asn
				20				25			30				

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
				35		40				45					

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
				50		55		60							

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
65					70			75			80				

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	His	Tyr	Asn	Asn	Trp	Ile	Thr
					85			90		95					

Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys						
				100		105									

<210> SEQ ID NO 145

<211> LENGTH: 357

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 145

caggtgcagc	tggtgcaagtc	tgggggaggc	tgggtcaagc	ctggagggtc	cctgagactc	60									
tcctgtgcag	cctctggatt	cacccatcgat	gactactaca	tgagctggat	ccgccaggct	120									
ccagggaaagg	ggctggagtg	ggtttccatac	attagttata	ctggtaggac	cataactac	180									
gccccactctg	tgaagggccg	attcaccatc	tccagggaca	acgccaagaa	ctcactgtat	240									
ctgcaaatgt	acagccctgag	agccgaggac	acggccgtgt	attactgtgc	gagagatacg	300									
gactacggtg	acttcttga	ctactgggc	cagggAACCC	tggtcaccgt	ctcctca	357									

<210> SEQ ID NO 146

<211> LENGTH: 119

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 146

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Gly
1					5			10			15				

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asp	Tyr
					20			25		30					

Tyr	Met	Ser	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
					35			40		45					

Ser	Tyr	Ile	Ser	Tyr	Thr	Gly	Arg	Thr	Ile	Tyr	Tyr	Ala	Asp	Ser	Val
					50			55		60					

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
65					70			75			80				

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90		95					

Ala	Arg	Asp	Thr	Asp	Tyr	Gly	Asp	Phe	Phe	Asp	Tyr	Trp	Gly	Gln	Gly
					100			105		110					

Thr	Leu	Val	Thr	Val	Ser	Ser									
					115										

<210> SEQ ID NO 147

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<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 147

ggattcacct tcagtgacta ctac

24

<210> SEQ ID NO 148
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 148

Gly Phe Thr Phe Ser Asp Tyr Tyr
1 5

<210> SEQ ID NO 149
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 149

attagttata ctggtaggac cata

24

<210> SEQ ID NO 150
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 150

Ile Ser Tyr Thr Gly Arg Thr Ile
1 5

<210> SEQ ID NO 151
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 151

gcgagagata cggactacgg tgacttcttt gactac

36

<210> SEQ ID NO 152
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 152

Ala Arg Asp Thr Asp Tyr Gly Asp Phe Phe Asp Tyr
1 5 10

<210> SEQ ID NO 153
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 153

gccatccaga	tgaccaggc	tccatcctca	ctgtctgcat	ctgttaggaga	cagagtacc	60
atcaacttgc	ggcgagtc	gggcattagc	aattattn	cctggttca	gcagaaacca	120
ggaaaagccc	ctaagtccct	gatctatgt	gcatccagt	tgcaaagtgg	ggtccccatca	180
aagttcagcg	gcagtggtc	tggcacat	ttcactctca	ccatcagcag	cctgcagcct	240
gaagattttg	caacttatta	ctgccaacag	tataatagt	acccgtcac	tttcggcgga	300
gggaccaagg	tggagatcaa	acga				324

<210> SEQ ID NO 154

<211> LENGTH: 108

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 154

Ala	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1						5		10				15			

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Asn	Tyr
		20					25				30				

Leu	Ala	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Ser	Leu	Ile
		35				40				45					

Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Lys	Phe	Ser	Gly
					50		55		60						

Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
					65		70		75				80		

Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Ser	Tyr	Pro	Leu
					85			90		95					

Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg					
					100			105							

<210> SEQ ID NO 155

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 155

cagggcatta	gcaattat														18
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<210> SEQ ID NO 156

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 156

Gln	Gly	Ile	Ser	Asn	Tyr										
1					5										

<210> SEQ ID NO 157

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 157

gctgcattcc

9

<210> SEQ_ID NO 158
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 158

Ala Ala Ser
1

<210> SEQ_ID NO 159
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 159

caaacatata atagttaccc gctcact

27

<210> SEQ_ID NO 160
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 160

Gln Gln Tyr Asn Ser Tyr Pro Leu Thr
1 5

<210> SEQ_ID NO 161
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 161

cagggtcagc tggtgagtc tgggggaggc ttggtaagc ctggagggtc cctgagactc	60
tccctgtcgac cctctggatt cacctttagt gactactaca tgagctggat ccgccaggct	120
ccagggaaagg ggctggagtg ggttcatac attagttata ctggtaggac cataactac	180
gcggactctg tgaaggcccg attaccatc tccagggaca acgccaagaa ctcactgtat	240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatacg	300
gactacggtg acttctttga ctactggggc cagggAACCC tggcacccgt ctcctca	357

<210> SEQ_ID NO 162
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 162

Gln Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr

-continued

20	25	30
----	----	----

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Tyr Thr Gly Arg Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Thr Asp Tyr Gly Asp Phe Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 163

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 163

gacatccaga tgaccaggc	tccatcctca ctgtctgc	ctgttaggaga cagagtacc	60
atcaacttgc gggcgagtca	gggcatttgc aattat	ttgcgttca gcagaaacca	120
ggaaaagccc ctaagtcct	gtatctatgc tgcata	aaatgtgg ggtcccatca	180
aatgttcagcg gcagtggatc	tggcacatgc ttca	ccatcagcag cctgcagc	240
gaagattttgc aacttatta	ctgccaacag tataat	atgtt acccgctcac tttcggc	300
gggaccaagg tggagatcaa	a		321

<210> SEQ ID NO 164

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 164

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly			
1	5	10	15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr			
20	25	30	

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile			
35	40	45	

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly			
50	55	60	

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
65	70	75	80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Leu			
85	90	95	

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 165

<211> LENGTH: 357

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

US 9,402,898 B2

119**120**

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<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 165

caggtgcagc	tggtgaggc	tgggggaggc	ttggtcaagc	ctggagggtc	cctgagactc	60
tccctgtcgac	cctctggatt	cacccatgt	gactactaca	tgagctggat	ccgccaggct	120
ccagggaaagg	ggctggagtg	ggtttcatac	attagttata	ctggtaggac	cataactac	180
gcagactctg	tgaaggggcc	attcaccatc	tccagggaca	acgccaagaa	ctcaactgtat	240
ctgcaaatga	acagecctgag	agccgaggac	acggccgtgt	attactgtgc	gagagatacg	300
gactacggtg	acttcttga	ctactgggc	cagggAACCC	tggtcaccgt	ctccctca	357

<210> SEQ ID NO 166

<211> LENGTH: 119

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 166

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Ley	Val	Lys	Pro	Gly	Gly
1							5			10			15		

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asp	Tyr
								20		25		30			

Tyr	Met	Ser	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
								35		40		45			

Ser	Tyr	Ile	Ser	Tyr	Thr	Gly	Arg	Thr	Ile	Tyr	Tyr	Ala	Asp	Ser	Val
							50		55		60				

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
							65		70		75		80		

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
							85		90			95			

Ala	Arg	Asp	Thr	Asp	Tyr	Gly	Asp	Phe	Phe	Asp	Tyr	Trp	Gly	Gln	Gly
							100		105			110			

Thr	Leu	Val	Thr	Val	Ser	Ser									
							115								

<210> SEQ ID NO 167

<211> LENGTH: 322

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 167

gacatccaga	tgacccagtc	tccatcctca	ctgtctgcat	ctgttaggaga	cagagtccacc	60
atcacttgtc	gggcgagtca	gggcattagc	aattatttag	cctggtttca	gcagaaaacca	120
ggaaaaagccc	ctaagtccct	gatctatgt	gcatccagg	tgcaaagtgg	ggtccccatca	180
aggttcagcg	gcagtggatc	tggcacat	ttcactctca	ccatcagcag	cctgcagcct	240
gaagatTTG	caacttatta	ctgccaacag	tataatagt	acccgctcac	tttcggcgga	300
gggaccaagg	tggagatcaa	ac				322

<210> SEQ ID NO 168

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 168

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1			5			10						15			
Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Gly	Ile	Ser	Asn	Tyr
	20					25						30			
Leu	Ala	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Ser	Leu	Ile
	35					40					45				
Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55				60					
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
	65				70				75					80	
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Ser	Tyr	Pro	Leu
					85				90			95			
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys					
					100				105						

<210> SEQ_ID NO 169

<211> LENGTH: 360

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 169

cagggtgcagc	tgggtcagtc	ggggggagac	gtgggtccagc	ctggggaggc	cctgagactc	60
tcctgtgcag	cgtctggatt	caccttca	agtatggca	tgcactgggt	ccgcccaggct	120
ccaggcaagg	gactggagtg	ggtggcaatt	atatggat	atggaaagtaa	taaatattat	180
gcagactccg	tgaaggggccg	attcaccatc	tccagagaca	attccaagaa	cacgcatttat	240
ctccaaatga	acagcctgag	agtcgaggac	acggctgtgt	actcctgtgc	gagagat	300
agtatatcat	ctcgccactt	tgactattgg	ggccaggaa	ccctggcac	cgtctccctca	360

<210> SEQ_ID NO 170

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 170

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Gly	Asp	Val	Val	Gln	Pro	Gly	Arg
1				5			10					15			
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
	20				25						30				
Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40					45					
Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50				55					60					
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
	65				70				75			80			
Leu	Gln	Met	Asn	Ser	Leu	Arg	Val	Glu	Asp	Thr	Ala	Val	Tyr	Ser	Cys
					85				90			95			
Ala	Arg	Asp	Phe	Ser	Ile	Ser	Ser	Arg	His	Phe	Asp	Tyr	Trp	Gly	Gln
					100				105			110			
Gly	Thr	Leu	Val	Thr	Val	Ser	Ser								
					115				120						

-continued

<210> SEQ_ID NO 171
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 171

ggattcacct tcagtagtta tggc

24

<210> SEQ_ID NO 172
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 172

Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> SEQ_ID NO 173
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 173

atatggtatg atggaagtaa taaa

24

<210> SEQ_ID NO 174
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 174

Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> SEQ_ID NO 175
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 175

gcgagagatt ttagtatatc atctcgccac tttgactat

39

<210> SEQ_ID NO 176
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 176

Ala Arg Asp Phe Ser Ile Ser Ser Arg His Phe Asp Tyr
1 5 10

<210> SEQ_ID NO 177
<211> LENGTH: 324

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 177

gacatccaga tgaccagtc tccatcctct ctgtctgcat ctgttaggaga cagagtacc	60
atcacttgtc gggcgagtca ggccattaac aattatttag cctggttca gcagaaacca	120
gggaaaagccc ctaagtccct gatctatgat acatccaatt tgcaaagtgg ggtcccttca	180
cagttcagcg gcagtggtatc tgggacagat tacactctca ccatcagcag cctgcaggct	240
gaagagtttg caacttattta ctgccaacag tattatattt acccgatcac cttcggccaa	300
gggacacgac tggagattaa acga	324

<210> SEQ ID NO 178
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 178

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly			
1	5	10	15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ala Ile Asn Asn Tyr			
20	25	30	
Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile			
35	40	45	
Tyr Ala Thr Ser Asn Leu Gln Ser Gly Val Pro Ser Gln Phe Ser Gly			
50	55	60	
Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro			
65	70	75	80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Ile Tyr Pro Ile			
85	90	95	
Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg			
100	105		

<210> SEQ ID NO 179
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 179

caggccatta acaattat	18
---------------------	----

<210> SEQ ID NO 180
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 180

Gln Ala Ile Asn Asn Tyr	
1	5

<210> SEQ ID NO 181
<211> LENGTH: 9
<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 181

gctacatcc

9

<210> SEQ ID NO 182
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 182

Ala Thr Ser
1

<210> SEQ ID NO 183
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 183

caacagtatt atatttaccc gatcacc

27

<210> SEQ ID NO 184
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 184

Gln Gln Tyr Tyr Ile Tyr Pro Ile Thr
1 5

<210> SEQ ID NO 185
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 185

caggtgcagc tggtgaggc tgggggagac gtggtccagc ctggggaggc cctgagactc	60
tccctgtgcag cgtctggatt caccttcagt agttatggca tgcactgggt ccgccaggct	120
ccaggcaagg gactggagtg ggtggcaatt atatggatg atggaaagtaa taaatattat	180
gcagactccg tgaaggccc attcaccatc tccagagaca attccaagaa cacgctttat	240
ctccaaatga acagectgag agtcgaggac acggctgtgt actcctgtgc gagagatTT	300
agtatatcat ctcgccactt tgactattgg ggccaggaa ccctggcac cgtctcccta	360

<210> SEQ ID NO 186
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 186

Gln Val Gln Leu Val Glu Ser Gly Asp Val Val Gln Pro Gly Arg

129**130**

-continued

1	5	10	15												
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
			20			25			30						
Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35			40			45								
Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50			55			60								
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65				70			75			80					
Leu	Gln	Met	Asn	Ser	Leu	Arg	Val	Glu	Asp	Thr	Ala	Val	Tyr	Ser	Cys
	85				90			95							
Ala	Arg	Asp	Phe	Ser	Ile	Ser	Ser	Arg	His	Phe	Asp	Tyr	Trp	Gly	Gln
	100				105				110						
Gly	Thr	Leu	Val	Thr	Val	Ser	Ser								
	115			120											

<210> SEQ ID NO 187

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 187

gacatccaga	tgaccaggc	tccatccctc	ctgtctgcat	ctgttaggaga	cagagtccacc	60
atcaattgtc	gggcgagtca	ggccattaac	aattatttag	cctgggttca	gcagaaacca	120
gggaaagccc	ctaagtccct	gatctatgct	acatccaatt	tgcaaagtgg	ggtccttca	180
cagttcagcg	gcagtggtac	tggcacat	tacactctca	ccatcagcag	cctgcagcct	240
gaagattttg	caacttatta	ctgccaacag	tattatattt	acccgatcac	cttcggccaa	300
gggacacgac	tggagattaa	a				321

<210> SEQ ID NO 188

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 188

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1			5			10				15					
Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ala	Ile	Asn	Asn	Tyr
	20				25			30							
Leu	Ala	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Ser	Leu	Ile
	35				40			45							
Tyr	Ala	Thr	Ser	Asn	Leu	Gln	Ser	Gly	Val	Pro	Ser	Gln	Phe	Ser	Gly
	50				55			60							
Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
65				70			75			80					
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Tyr	Ile	Tyr	Pro	Ile
	85				90					95					
Thr	Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys					
	100			105											

<210> SEQ ID NO 189

<211> LENGTH: 360

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 189

```
caggtgcagc tggtgaggc tgggggaggc gtggtccagc ctgggaggc cctgagactc      60
tcctgtgcag cgtctggatt caccttcagt agttatggca tgcaactgggt ccgccaggct    120
ccaggcaagg ggcttagatg ggtggcagtt atatggatg atggaaatgaa taaatactat     180
gcagactccg tgaaggggccg attaccatc tccagagaca attccaagaa cacgtgtat     240
ctgc当地atgaa acagectgag agccgaggac acggctgtgt attactgtgc gagagatTTT   300
agtatatcat ctc当地actt tgactattgg ggccaggaa ccctggtcac cgtctccctca   360
```

<210> SEQ ID NO 190
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 190

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1           5           10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20          25           30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35          40           45

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50          55           60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70           75           80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85          90           95

Ala Arg Asp Phe Ser Ile Ser Ser Arg His Phe Asp Tyr Trp Gly Gln
100         105          110

Gly Thr Leu Val Thr Val Ser Ser
115         120
```

<210> SEQ ID NO 191
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 191

```
gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgttaggaga cagagtccacc    60
atcacttgtc gggcgagtca ggccattaac aattattag cctggttca gcagaaacca    120
gggaaaagccc ctaagtccct gatctatgct acatccagtt tgcaaagtgg ggtcccatca   180
aggttcagcg gcagtggtc tgggacatg ttcaactctca ccatcagcag cctgcagcct   240
gaagatTTT caacttatta ctgccaacag tattatattt acccgatcac cttcggccaa   300
gggacacgac tggagattaa ac                         322
```

<210> SEQ ID NO 192
<211> LENGTH: 107
<212> TYPE: PRT

-continued

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 192

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly
1															
							5			10				15	

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ala	Ile	Asn	Asn	Tyr
				20				25				30			

Leu	Ala	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Ser	Leu	Ile
				35		40				45					

Tyr	Ala	Thr	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
				50		55		60							

Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
				65		70		75		80					

Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Tyr	Ile	Tyr	Pro	Ile
				85		90				95					

Thr	Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys					
										100					
								105							

<210> SEQ ID NO 193

<211> LENGTH: 372

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 193

gaggtgcagc	tggtgaggc	tgggggaggc	gtggtccagc	ctgggaggc	cctgagactc		60
tcctgtcgac	cgtctggatt	caccttcagt	agctatggca	tgcactgggt	ccgccaggct		120
ccagacaagg	ggctggagtg	ggtggcagtt	aaatggatg	atggaagtaa	taaatattat		180
gcagactccg	tgaaggccg	attcaccatc	tccagagaca	attccaagaa	cacgctgtat		240
ctgcaaatga	acagcctgag	agccgaggac	acggctgtgt	attactgtgc	gagagaaggc		300
ccttacgatt	tttacagtgg	ttatggagct	tttgatatct	ggggccaagg	gacaatggc		360
accgtctctt	ca						372

<210> SEQ ID NO 194

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 194

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1														
								5		10		15		

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
				20			25		30						

Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Asp	Lys	Gly	Leu	Glu	Trp	Val
				35			40		45						

Ala	Val	Lys	Trp	Asp	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
				50			55		60						

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
				65			70		75		80				

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85			90		95						

-continued

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp
 100 105 110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 195
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 195

ggattcacct tcagtagcta tggc 24

<210> SEQ ID NO 196
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 196

Gly Phe Thr Phe Ser Ser Tyr Gly
 1 5

<210> SEQ ID NO 197
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 197

aaatggatg atggaagtaa taaa 24

<210> SEQ ID NO 198
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 198

Lys Trp Asp Asp Gly Ser Asn Lys
 1 5

<210> SEQ ID NO 199
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 199

gcgagagaag gcccttacga ttttacagt ggttatggag cttttatat c 51

<210> SEQ ID NO 200
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 200

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp

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1	5	10	15
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Ile

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<210> SEQ ID NO 201
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 201
gacatccaga tgaccaggc tccatcctca ctgtctgc ctgttaggaga cagagtccacc      60
atcacttgtc gggcgagtca gggcattagc aattatttag cctggtttca gcagaaacca      120
ggaaaaagccc ctaagtccct gatctatgc gcatccaggc tgcaaagtgg ggtccccatca      180
aagttcagcg gcagtggtatc tgggacagat ttcactctca ccatcagcag cctgcagcct      240
gaagattttg caacttatta ctgccaacag tataatagtt accctcggac gttcggccaa      300
gggaccaagg tggagatcaa acga                                         324

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<210> SEQ ID NO 202
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 202
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1           5           10          15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20          25          30

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35          40          45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
50          55          60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65          70          75          80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Arg
85          90          95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100         105

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<210> SEQ ID NO 203
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 203
cagggcattta gcaattat

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<210> SEQ ID NO 204
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 204

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18

-continued

Gln Gly Ile Ser Asn Tyr
1 5

<210> SEQ ID NO 205
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 205

gctgcatcc

9

<210> SEQ ID NO 206
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 206

Ala Ala Ser
1

<210> SEQ ID NO 207
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 207

caacagtata atagttaccc tcggacg

27

<210> SEQ ID NO 208
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 208

Gln Gln Tyr Asn Ser Tyr Pro Arg Thr
1 5

<210> SEQ ID NO 209
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 209

cagggtgcagc	tggtgaggtc	tgggggaggc	gtgggtccagc	ctggggaggc	cctgagactc	60
tcctgtgcag	cgtctggatt	caccttcagt	agctatggca	tgcactgggt	ccgccaggct	120
ccagacaagg	ggctggagtg	ggtggcagtt	aaatggatg	atggaagtaa	taaatattat	180
cgagactccg	tgaagggccg	attcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagccttag	agccgaggac	acggctgtgt	attactgtgc	gagagaaggc	300
ccttacgatt	tttacagtgg	ttatggagct	tttgatatct	ggggccaagg	gacaatggc	360
accgtctctt	ca					372

<210> SEQ ID NO 210

-continued

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<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 210

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
1           5          10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20          25          30

Gly Met His Trp Val Arg Gln Ala Pro Asp Lys Gly Leu Glu Trp Val
35          40          45

Ala Val Lys Trp Asp Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50          55          60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70          75          80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp
100         105         110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115         120

<210> SEQ ID NO 211
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 211

gacatccaga tgaccaggc tccatcctca ctgtctgc cat ctgttaggaga cagagtccacc      60
atcacttgtc gggcgagtca gggcatttgc aatttttag cctggttca gcagaaaccca      120
gggaaaagccc ctaagtcctt gatctatgtc gcatccagg ttgaaatgtgg ggtcccatca      180
aagttcagcg gcagtggtatc tgggacatgat ttcactctca ccatcagcag cctgcagcc      240
gaagattttt caacttatta ctgccaacag tataataggat accctcgac gttcggccaa      300
gggaccaagg tggaaatcaa a                                         321

<210> SEQ ID NO 212
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 212

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1           5          10          15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr
20          25          30

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35          40          45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
50          55          60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65          70          75          80

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Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Ser	Tyr	Pro	Arg
85								90						95	

Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys
	100							105		

<210> SEQ ID NO 213
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 213

caggtgcagc	tggtgaggc	tgggggaggc	gtgggtccagc	ctggggaggc	cctgagactc	60
tccctgtcgac	cgtctggatt	cacccatgt	agctatggca	tgcactgggt	ccgccaggct	120
ccaggcaagg	ggcttagagt	ggtggcagtt	aatgggatg	atggaaagtaa	taaatactat	180
gcagactccg	tgaaggggccg	attcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggctgtgt	attactgtgc	gagagaaggc	300
ccttacgatt	tttacagtgg	ttatggagct	tttgatatct	ggggccaagg	gacaatggc	360
accgtctctt	ca					372

<210> SEQ ID NO 214
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 214

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1					5			10				15			
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
					20			25				30			
Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40				45						
Ala	Val	Lys	Trp	Asp	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50				55				60						
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
	65				70			75			80				
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
			85			90			95						
Ala	Arg	Glu	Gly	Pro	Tyr	Asp	Phe	Tyr	Ser	Gly	Tyr	Gly	Ala	Phe	Asp
	100				105				110						
Ile	Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser				
	115				120										

<210> SEQ ID NO 215
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 215

gacatccaga	tgaccaggc	tccatccctca	ctgtctgcac	ctgttaggaga	cagagtccacc	60
atcacttgtc	gggcgagtc	gggcattagc	aattatttag	cctggtttca	gcagaaacca	120
gggaaagccc	ctaagtccct	gatctatgtc	gcatccagg	tgcaaagtgg	ggtccccatca	180

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aggttcagcg gcagtggatc tggacagat ttcaactctca ccatcagcag cctgcagcct	240
gaagatttg caacttatta ctgccaacag tataatagtt accctcgac gttcggccaa	300
gggaccaagg tggaaatcaa ac	322

<210> SEQ ID NO 216

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 216

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly	
1 5 10 15	

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Asn Tyr	
20 25 30	

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile	
35 40 45	

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro	
65 70 75 80	

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Pro Arg	
85 90 95	

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
100 105	

<210> SEQ ID NO 217

<211> LENGTH: 372

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 217

gaggtgcagc tgggtcagtc tgggggaggc gtgggtccagc ctggggaggc cctgagactc	60
tccctgtcag cgtctggatt cacttcagt agctatggca tgcactgggt ccggcaggct	120
ccagacaagg ggctggagtg ggtggcagtt aaatggatg atggaaatggtaaaatattat	180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgc当地atga acagectgag agccgaggac acggctgtgtt attactgtgc gagagaaggc	300
ccttacgatt ttacagttt gatggagct tttgatatctt gggccaagg gacaatggtc	360
accgtctctt ca	372

<210> SEQ ID NO 218

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 218

Glu Val Gln Leu Val Gln Ser Gly Gly Val Val Gln Pro Gly Arg	
1 5 10 15	

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr	
20 25 30	

Gly Met His Trp Val Arg Gln Ala Pro Asp Lys Gly Leu Glu Trp Val

-continued

35 40 45

Ala Val Lys Trp Asp Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp
100 105 110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 219
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 219

ggattcacct tcagtagcta tggc

24

<210> SEQ ID NO 220
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 220

Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> SEQ ID NO 221
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 221

aaatgggatg atggaagtaa taaa

24

<210> SEQ ID NO 222
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 222

Lys Trp Asp Asp Gly Ser Asn Lys
1 5

<210> SEQ ID NO 223
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 223

gcgagagaag gcccttacga ttttacagt ggttatggag ctttgatat c

51

-continued

<210> SEQ ID NO 224
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 224

Ala	Arg	Glu	Gly	Pro	Tyr	Asp	Phe	Tyr	Ser	Gly	Tyr	Gly	Ala	Phe	Asp
1				5				10					15		

Ile

<210> SEQ ID NO 225
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 225

gacatccagt	tgaccaggc	tccaggcacc	ctgtctttgt	ctccagggga	aagagccacc	60
ctctcctgca	gggcaggta	gagtgttagc	agcagctact	tagcctggta	ccagcagaaa	120
cctggccagg	ctcccaggct	cctcatctat	ggtgcatcca	gcagggcac	tggcatccca	180
gacaggttca	gtggcagtgg	gtctggaca	gacttcactc	tcaccatcag	cagactggag	240
cctgaagatt	ttgcagtgt	taactgttag	cagtatggta	gtcactcac	tttcggcgga	300
gggaccaagc	tggagatcaa	acgaa				324

<210> SEQ ID NO 226
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 226

Asp	Ile	Gln	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1				5				10				15			

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Ser
				20				25				30			

Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
				35				40				45			

Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
				50				55				60			

Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
				65				70				75			80

Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Gly	Ser	Ser	Leu
				85				90				95			

Thr	Phe	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg					
				100				105							

<210> SEQ ID NO 227
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 227

cagagtgtta gcagcagcta c

-continued

<210> SEQ_ID NO 228
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 228

Gln Ser Val Ser Ser Ser Tyr
1 5

<210> SEQ_ID NO 229
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 229

ggtgcatcc

9

<210> SEQ_ID NO 230
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 230

Gly Ala Ser
1

<210> SEQ_ID NO 231
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 231

cagcagtatg gtagtcact cact

24

<210> SEQ_ID NO 232
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 232

Gln Gln Tyr Gly Ser Ser Leu Thr
1 5

<210> SEQ_ID NO 233
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 233

cagggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggagggtc cctgagactc 60
tcctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120
ccagacaagg ggctggagtg ggtggcagtt aaatggatg atggaagtaa taaatattat 180

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gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagaaggc      300
ccttacgatt ttacagtgg ttatggagct ttgatatatct ggggccaagg gacaatggc      360
accgtctctt ca                                         372

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<210> SEQ ID NO 234
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 234

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
1           5           10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20          25          30

Gly Met His Trp Val Arg Gln Ala Pro Asp Lys Gly Leu Glu Trp Val
35          40          45

Ala Val Lys Trp Asp Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50          55          60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70          75          80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp
100         105         110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115         120

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<210> SEQ ID NO 235
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 235

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgcg gggccagtca gagtgtagc agcagctact tagcctggta ccagcagaaa      120
cctggccagg ctcaggct cctcatctat ggtgcataccca gcagggccac tggcatccca      180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag      240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gtcactcac ttccggcgga      300
gggaccaagg tggagatcaa a                                         321

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<210> SEQ ID NO 236
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 236

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1           5           10          15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser

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20	25	30	
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu			
35	40	45	
Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser			
50	55	60	
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu			
65	70	75	80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu			
85	90	95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 237

<211> LENGTH: 372

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 237

cagggtgcagc tgggtggagtc tgggggaggc gtgggtccagc ctggggaggc cctgagactc	60
tccctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggccaagg ggcttagagtg ggtggcagtt aaatggatg atggaaagtaa taaatactat	180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgc当地atga acagecctgag agccgaggac acggctgtgt attactgtgc gagagaaggc	300
ccttacgatt ttacagtggt ttatggagct tttgatatct ggggccaagg gacaatggtc	360
accgtctctt ca	372

<210> SEQ ID NO 238

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 238

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg			
1	5	10	15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr		
20	25	30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val		
35	40	45

Ala Val Lys Trp Asp Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val		
50	55	60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
65	70	75	80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys		
85	90	95

Ala Arg Glu Gly Pro Tyr Asp Phe Tyr Ser Gly Tyr Gly Ala Phe Asp		
100	105	110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser	
115	120

<210> SEQ ID NO 239

<211> LENGTH: 322

<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 239

```
gaaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgca gggccagtc gagtgtttgc agcagctact tagcctggta ccagcagaaa     120
cctggccagg ctcccaggct cctcatctat ggtgcattca gcagggccac tggcatccca     180
gacaggttca gtggcagtgg gtctggaca gacttcactc tcaccatcag cagactggag    240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gtcactcac tttcggcgga    300
gggaccaagg tggagatcaa ac                                         322
```

<210> SEQ_ID NO 240
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 240

Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Gly	Thr	Leu	Ser	Leu	Ser	Pro	Gly
1															
															15

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Ser
															30
20															

Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu
35															
															45

Ile	Tyr	Gly	Ala	Ser	Ser	Arg	Ala	Thr	Gly	Ile	Pro	Asp	Arg	Phe	Ser
50															
															60

Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Arg	Leu	Glu
65															
															80

Pro	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Gly	Ser	Ser	Leu
85															
															95

Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys					
100															
															105

<210> SEQ_ID NO 241
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 241

```
gagggtcaat tggggaggc gggggggggc ttggtaaggc cggggggggc ccttagactc      60
tcctgtcag cctctggatt cacttcaact aacgcctggta tgagctgggt ccggccaggct     120
ccagggaaagg ggctggaggc gattggccag attaaaagca aaactgtatgg tgggacaata     180
gactacgctg cacccgtgaa aggccatcc accgtctcaa gagatgatcc agaaaatacc     240
ctgtttctgc aatgaacacg cctgaaaacc gaggacacag ccgtgtatcc ctgtgcgggg     300
aactggaact acgtggactt tgactactgg ggccaggaa ccctggcac cgtctccctca     360
```

<210> SEQ_ID NO 242
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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-continued

<400> SEQUENCE: 242

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Arg	Pro	Gly	Gly
1					5			10				15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Thr	Asn	Ala
	20				25				30						

Trp	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Ile
	35				40				45						

Gly	Gln	Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Ile	Asp	Tyr	Ala	Ala
	50				55			60							

Pro	Val	Lys	Gly	Arg	Phe	Thr	Val	Ser	Arg	Asp	Asp	Ser	Glu	Asn	Thr
65					70			75		80					

Leu	Phe	Leu	Gln	Met	Asn	Ser	Leu	Lys	Thr	Glu	Asp	Thr	Ala	Val	Tyr
	85				90				95						

Tyr	Cys	Ala	Gly	Asn	Trp	Asn	Tyr	Val	Asp	Phe	Asp	Tyr	Trp	Gly	Gln
	100					105			110						

Gly	Thr	Leu	Val	Thr	Val	Ser	Ser								
	115				120										

<210> SEQ_ID NO 243

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 243

ggattcactt tcactaacgc ctgg

24

<210> SEQ_ID NO 244

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 244

Gly	Phe	Thr	Phe	Thr	Asn	Ala	Trp								
1					5										

<210> SEQ_ID NO 245

<211> LENGTH: 30

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 245

ataaaaagca aaactgatgg tggggacaata

30

<210> SEQ_ID NO 246

<211> LENGTH: 10

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 246

Ile	Lys	Ser	Lys	Thr	Asp	Gly	Gly	Thr	Ile						
1					5		10								

<210> SEQ_ID NO 247

<211> LENGTH: 33

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-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 247

gcggggaaact ggaactacgt ggactttgac tac

33

<210> SEQ ID NO 248
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 248

Ala Gly Asn Trp Asn Tyr Val Asp Phe Asp Tyr
1 5 10

<210> SEQ ID NO 249
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 249

gacatccaga tgacctcagtc tccatccctcc ctgtctgcat ctgttaggaga cagagtacc	60
atcacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca	120
gggaaaagccc ctaagcgccct gatctatgct gcatccagg tgcaagggtgg ggtcccatca	180
aggttccagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct	240
gaagattttgc aacttattta ctgtctacag cataatagtt accctttcac tttcgccct	300
gggaccaaag tggatatcaa a	321

<210> SEQ ID NO 250
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 250

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
20 25 30Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45Tyr Ala Ala Ser Ser Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Phe
85 90 95Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> SEQ ID NO 251
<211> LENGTH: 18
<212> TYPE: DNA

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
<400> SEQUENCE: 251

caggacatta gaaatgat

18

<210> SEQ ID NO 252
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 252

Gln Asp Ile Arg Asn Asp
1 5

<210> SEQ ID NO 253
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 253

gctgcattcc

9

<210> SEQ ID NO 254
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 254

Ala Ala Ser
1

<210> SEQ ID NO 255
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 255

ctacagcata atagttaccc tttcact

27

<210> SEQ ID NO 256
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 256

Leu Gln His Asn Ser Tyr Pro Phe Thr
1 5

<210> SEQ ID NO 257
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 257

```

gaggtgcagc tggtggagtc tgggggaggc ttggtaaggc cgggggggtc ccttagactc      60
tcctgtcag cctctggatt cacttcaact aacgcctgga tgagctgggt ccgccaggct      120
ccagggaaagg ggctggagtg gattggccag attaaaagca aaactgtatgg tgggacaata      180
gactacgctg caccgtgaa aggagattc accgtctcaa gagatgttc agaaaatacg      240
ctgtttctgc aatgaacag cctgaaaacc gaggacacag ccgtgtattha ctgtgcgggg      300
aactggaaact acgtggactt tgactactgg ggccagggaa ccctggcac cgctccctca      360

```

<210> SEQ ID NO 258

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 258

```

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Arg Pro Gly Gly
1           5           10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Asn Ala
20          25          30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35          40          45

Gly Gln Ile Lys Ser Lys Thr Asp Gly Gly Thr Ile Asp Tyr Ala Ala
50          55          60

Pro Val Lys Gly Arg Phe Thr Val Ser Arg Asp Asp Ser Glu Asn Thr
65          70          75          80

Leu Phe Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85          90          95

Tyr Cys Ala Gly Asn Trp Asn Tyr Val Asp Phe Asp Tyr Trp Gly Gln
100         105         110

Gly Thr Leu Val Thr Val Ser Ser
115         120

```

<210> SEQ ID NO 259

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 259

```

gacatccaga tgacctagtc tccatccctcc ctgtctgcat ctgttaggaga cagagtcacc      60
atcaacttgcc gggcaagtca ggacattaga aatgatttag gctggtatca gcagaaacca      120
ggaaaagccc otaagcgcc t gatctatgct gcatccagg t gcaagg tgg ggtcccatca      180
agg ttcagcg gca gatggatc tggcagacaa ttcaactctca caatcagcag cctgcagcct      240
gaagat tttg caacttatta ctgtctacag cataatagt accctttcac tttcggccct      300
gggaccaaa g tggatata a a

```

321

<210> SEQ ID NO 260

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 260

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-continued

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
 20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Phe
 85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

<210> SEQ ID NO 261

<211> LENGTH: 360

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 261

gaggtgcagc tggtgaggc tgggggagc ttggtaaacgc ctggggggtc ccttagactc 60
 tcctgtgcag cctctggatt cacttcaact aacgcctggc tgagctgggt ccgccaggct 120
 ccagggaaagg ggctggagtg ggttggccgt attaaaagca aaactgatgg tgggacaata 180
 gactacgctg caccctgtgaa aggcagattc accatctcaa gagatgattc aaaaaacacg 240
 ctgttatctgc aaatgaacag cctgaaaacc gaggacacag ccgtgtattha ctgtgcgggg 300
 aactggaact acgtggactt tgactactgg ggccagggaa ccctggtcac cgtctcccta 360

<210> SEQ ID NO 262

<211> LENGTH: 120

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 262

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Asn Ala
 20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Ile Asp Tyr Ala Ala
 50 55 60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

Tyr Cys Ala Gly Asn Trp Asn Tyr Val Asp Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

-continued

```

<210> SEQ ID NO 263
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 263

gacatccaga tgaccaggc tccatccctcc ctgtctgcat ctgttaggaga cagagtccacc      60
atcaatttgc gggcaagtca ggacattaga aatgatttag gctggatca gcagaaacca      120
ggaaaagccc ctaagcgctt gatctatgtt gcatccagg tgcggatgg ggtcccatca      180
agtttcagcg gcagtggtatc ttcaacttc caatcagcag cctgcaggct      240
gaagattttt caacttatta ctgtctacag cataatagtt accctttcac tttcgccct      300
gggaccaaaag tggatataac ac      322

```

```

<210> SEQ ID NO 264
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 264

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1           5           10          15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Arg Asn Asp
20          25          30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35          40          45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50          55          60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65          70          75          80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ser Tyr Pro Phe
85          90          95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100         105

```

```

<210> SEQ ID NO 265
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 265

cagggtcagc tgggtggatc tggggggggc gtgggtccagc ctgggggggc cctgagactc      60
tccctgtcagc cgtctggatt caccctcagt aactatggca tgcactgggt ccggccaggct      120
ccaggcaagg ggctggatgc ggtggcagtt atatggcatg atggaaagtt tacataactat      180
gcagactccg tgaaggggccg attcaccatc tccagagaca attctaagaa cacgctgttat      240
ctgc当地atgc acagcctgag agccgaagac acggctgtgtt attactgtac gagagagggg      300
ctcgatcccc ggagtggatc ttaccctaac tgggtcgacc cctggggccca gggaaacctg      360
gtcaccgtct cctca      375

```

```

<210> SEQ ID NO 266
<211> LENGTH: 125

```

-continued

<212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

 <400> SEQUENCE: 266

 Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15

 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Asn Tyr
 20 25 30

 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

 Ala Val Ile Trp His Asp Gly Ser Asn Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

 Thr Arg Glu Gly Leu Asp Phe Trp Ser Gly Tyr Tyr Pro Asn Trp Phe
 100 105 110

 Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120 125

<210> SEQ ID NO 267
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

 <400> SEQUENCE: 267

 ggattcaccc tcagtaacta tggc

24

<210> SEQ ID NO 268
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 268

 Gly Phe Thr Leu Ser Asn Tyr Gly
 1 5

<210> SEQ ID NO 269
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 269

 atatggcatg atggaagtaa taca

24

<210> SEQ ID NO 270
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 270

Ile Trp His Asp Gly Ser Asn Thr

-continued

1 5

<210> SEQ ID NO 271
<211> LENGTH: 54
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 271

acgagagagg ggctcgattt ttggagtggt tattacccta actggttcga cccc 54

<210> SEQ ID NO 272
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 272

Thr Arg Glu Gly Leu Asp Phe Trp Ser Gly Tyr Tyr Pro Asn Trp Phe
1 5 10 15

Asp Pro

<210> SEQ ID NO 273
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 273

gacatccaga tgacctcagtc tccatccctcc ctgtctgcat ctgttaggaga cagagtacc 60
atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120
ggaaaaagccc ctaagcgctt gatctatgtt gcatccaattt tgcaagggtgg ggtcccatca 180
aggttcagcg gcagttggatc tgggacagaaa ttcaactctca caatcagcag cctgcagcct 240
gaagattttgc agcttattatctgtctacag cataatattt acccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> SEQ ID NO 274
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 274

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45Tyr Ala Ala Ser Asn Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80Glu Asp Phe Ala Ala Tyr Tyr Cys Leu Gln His Asn Ile Tyr Pro Leu
85 90 95

-continued

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 275
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 275

cagggcattt gaaatgat

18

<210> SEQ ID NO 276
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 276

Gln Gly Ile Arg Asn Asp
1 5

<210> SEQ ID NO 277
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 277

gctgcattt

9

<210> SEQ ID NO 278
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 278

Ala Ala Ser
1

<210> SEQ ID NO 279
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 279

ctacagcata atatttaccc gctcaact

27

<210> SEQ ID NO 280
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 280

Leu Gln His Asn Ile Tyr Pro Leu Thr
1 5

-continued

<210> SEQ ID NO 281
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 281

```
caggtgcagc tggtgaggc tgggggaggc gtggccagc ctgggaggc cctgagactc      60
tcctgtcgac cgtctggatt cacccctcagt aactatggca tgcaactgggt ccgccaggct    120
ccaggcaagg ggctggagtg ggtggcagtt atatggcatg atggaaagtaa tacatactat    180
gcagactccg tgaaggcccg attcaccatc tccagagaca attctaagaa cacgctgtat    240
ctgcaaatga acagectgag agccgaagac acggctgtgt attactgtac gagagagggg    300
ctcgattttt ggagtggta ttaccctaac tggttcgacc cctggggcca gggAACCTG    360
gtcacccgtct cctca                                         375
```

<210> SEQ ID NO 282
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 282

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1				5				10			15				

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Leu	Ser	Asn	Tyr
	20				25					30					

Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40					45					

Ala	Val	Ile	Trp	His	Asp	Gly	Ser	Asn	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
	50				55				60						

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
	65				70				75				80		

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
		85				90				95					

Thr	Arg	Glu	Gly	Leu	Asp	Phe	Trp	Ser	Gly	Tyr	Tyr	Pro	Asn	Trp	Phe
			100			105				110					

Asp	Pro	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser			
		115			120						125				

<210> SEQ ID NO 283
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 283

```
gacatccaga tgacctcagtc tccatccctcc ctgtctgcat ctgttaggaga cagagtcacc      60
atcacccgtcc gggcaagtca gggcattaga aatgatttag gtttgttatca gcagaaacca    120
ggaaaagccc ctaagcgccct gatctatgtt gcatccatt tgcaagggtgg ggtcccatca    180
aggttcagcg gcagttggatc tgggacagaa ttcactctca caatcagcag cctgcagcct    240
gaagattttg cagtttatta ctgtctacag cataataattt acccgctcac tttcggcgga    300
gggaccaagg tggagatcaa a                                         321
```

179

180

-continued

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<210> SEQ ID NO 284
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 284

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
20 25 30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Gln Gly Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Ala Tyr Tyr Cys Leu Gln His Asn Ile Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

```

```
<210> SEQ ID NO 285
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 285

cagggtgcagc tgggtggagtc tgggggagggc gtggtccagc ctgggagggtc cctgagactc 60
tccttgtgcag cgtctggatt caccctcagt aactatggca tgcactgggt ccgcaggct 120
ccaggccaagg ggcttagagtg ggtggcagtt atatggcatg atggaagtaa tacatactat 180
gcagactccg tgaagggcgcg attcaccatc tccagagaca attccaagaa cacgtgtat 240
ctgcaaatagtc acagcctgag agccgaggac acggctgtgt attachgtac gagagagggg 300
ctcgattttt ggagtggta ttaccctaact tggttcgacc cctggggcca gggAACCTG 360
gtcacccgtct cctca 375
```

```

<210> SEQ ID NO 286
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 286

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1           5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Ser Asn Tyr
20          25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35          40                  45

Ala Val Ile Trp His Asp Gly Ser Asn Thr Tyr Tyr Ala Asp Ser Val
50          55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70                  75                  80

```

-continued

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Glu Gly Leu Asp Phe Trp Ser Gly Tyr Tyr Pro Asn Trp Phe
100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 287

<211> LENGTH: 322

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 287

gacatccaga	tgacccagtc	tccatcctcc	ctgtctgcat	ctgttaggaga	cagagtacc	60
atcaacttgc	ggcaagtca	gggcattaga	aatgatttag	gctggtatca	gcagaaacca	120
ggaaaagccc	ctaagccct	gatctatgt	gcatccagt	tgcaaagtgg	ggtccatca	180
aggttcagcg	gcagtggtac	tggcacagaa	ttcactctca	caatcagcag	cctgcagcct	240
gaagattttg	caacttatta	ctgtctacag	cataatattt	acccgtcac	tttcggcgga	300
gggaccaagg	tggagatcaa	ac				322

<210> SEQ ID NO 288

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 288

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly			
1	5	10	15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp		
20	25	30

Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile		
35	40	45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
50	55	60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro			
65	70	75	80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Ile Tyr Pro Leu		
85	90	95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys		
100	105	

<210> SEQ ID NO 289

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 289

gaggtgcagc	tggggagtc	tggggagac	ttgggtccagc	ctgggggtc	cctgagactc	60
tcctgtacag	cctctggatt	cacctttagt	aaatattgga	tgacctgggt	ccgccaggct	120
ccagggaggg	ggctggagtg	ggtggccaac	ataaaggaag	atggaaatga	aaaatactt	180

-continued

ctggactctg tgaaggcccg cttcaccatt tccagagaca acgccaagga tttattgtt	240
ctgc当地atga acagecctgag aggegaggac acggctgtgt attactgtgt gagagatcga	300
ggtatagaag tggctggccc ctttgactac tggggccagg gaaccctggt caccgtctcc	360
tca	363

<210> SEQ ID NO 290
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 290

Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly	
1 5 10 15	
Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Lys Tyr	
20 25 30	
Trp Met Thr Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val	
35 40 45	
Ala Asn Ile Lys Glu Asp Gly Asn Glu Lys Tyr Phe Leu Asp Ser Val	
50 55 60	
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Leu Leu Phe	
65 70 75 80	
Leu Gln Met Asn Ser Leu Arg Gly Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	
Val Arg Asp Arg Gly Ile Glu Val Ala Gly Pro Phe Asp Tyr Trp Gly	
100 105 110	
Gln Gly Thr Leu Val Thr Val Ser Ser	
115 120	

<210> SEQ ID NO 291
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 291

ggattcacct ttagtaata ttgg	24
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<210> SEQ ID NO 292
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 292

Gly Phe Thr Phe Ser Lys Tyr Trp	
1 5	

<210> SEQ ID NO 293
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 293

ataaaggaag atggaaatga aaaa	24
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<210> SEQ ID NO 294
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 294

Ile Lys Glu Asp Gly Asn Glu Lys
1 5

<210> SEQ ID NO 295
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 295

gtgagagatc gaggtataga agtggctggc ccctttgact ac

42

<210> SEQ ID NO 296
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 296

Val Arg Asp Arg Gly Ile Glu Val Ala Gly Pro Phe Asp Tyr
1 5 10

<210> SEQ ID NO 297
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 297

gacatccaga tgacctagtc tccttccacc ctgtctgcat ctgttgaaaa cagagtccacc	60
gtcaacttgc gggccagtca gactattatt aattgggtgg cctggtatca gcagaaacca	120
gggaaaagccc ctaaactcct gatctctaag gcgtcttagt tagaaaatgg ggtccccatca	180
aggttcagcg gcagtggatc tggcacagaa ttcaacttca ccattagcag cctgcagcct	240
gtatgattttgc caacttattatc ctgccaacagataataggatttggacgtt cggccaagg	300
accatggtgg aaatcaaa	318

<210> SEQ ID NO 298
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 298

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Val Thr Cys Arg Ala Ser Gln Thr Ile Ile Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

187**188**

-continued

Ser Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Arg Tyr Trp Thr
85 90 95

Phe Gly Gln Gly Thr Met Val Glu Ile Lys
100 105

<210> SEQ ID NO 299
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 299

cagactattatataattgg

18

<210> SEQ ID NO 300
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 300

Gln Thr Ile Ile Asn Trp
1 5

<210> SEQ ID NO 301
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 301

aaggcgtct

9

<210> SEQ ID NO 302
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 302

Lys Ala Ser
1

<210> SEQ ID NO 303
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 303

caacagtata ataggtattt gacg

24

<210> SEQ ID NO 304
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 304

Gln Gln Tyr Asn Arg Tyr Trp Thr
 1 5

<210> SEQ ID NO 305
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 305

gagggtgcagc tgggggagtc tgggggagac ttgggtccagc ctggggggtc cctgagactc	60
tcctgtacag cctctggatt caccttagt aaatattgga tgacctgggt ccgccaggt	120
ccagggaggg ggctggagtg ggtggccaac ataaaggaag atggaaatga aaaatactt	180
ctggactctg tgaaggggccg cttcaccatt tccagagaca acggcaagga tttattgtt	240
ctgcaaatga acagcctgag aggcgaggac acggctgtgt attactgtgt gagagatcga	300
ggtatagaag tggctggccc ctttactac tggggccagg gaaccctggt caccgtctcc	360
tca	363

<210> SEQ ID NO 306
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 306

Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Ser Lys Tyr
 20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Arg Gly Leu Glu Trp Val
 35 40 45

Ala Asn Ile Lys Glu Asp Gly Asn Glu Lys Tyr Phe Leu Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Leu Leu Phe
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Gly Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Val Arg Asp Arg Gly Ile Glu Val Ala Gly Pro Phe Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 307
 <211> LENGTH: 318
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 307

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgtgggga cagagtacc	60
gtcacttgcc gggccagtca gactattatt aattgggttg cctggtatca gcagaaacca	120

-continued

gggaaagccc	ctaaactcct	gatctctaag	gcgtctagtt	tagaaagtgg	ggtcccatca	180
aggttcagcg	gcagtggatc	tggcacagaa	ttcactctca	ccattagcag	cctgcagcct	240
gatgatttg	caacttatta	ctgccaacag	tataatagg	attggacggtt	cggccaaggg	300
accaagggtgg	aaatcaa					318

<210> SEQ ID NO 308
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 308

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1							5		10					15	
Asp	Arg	Val	Thr	Val	Thr	Cys	Arg	Ala	Ser	Gln	Thr	Ile	Ile	Asn	Trp
	20						25					30			
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Ile	
	35					40					45				
Ser	Lys	Ala	Ser	Ser	Leu	Glu	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55					60				
Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro
	65					70					75			80	
Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Arg	Tyr	Trp	Thr
	85						90				95				
Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys						
	100						105								

<210> SEQ ID NO 309
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 309

gagggtgcagc	tggggagtc	tgggggaggc	ttgggtccagc	ctggggggtc	cctgagactc	60
tccctgtcgag	cctctggatt	caccttttagt	aaatattgga	ttagctgggt	ccgccaggct	120
ccagggaaagg	ggctggagtg	ggtgtggcaac	ataaaggaag	atggaaatga	aaaatactat	180
gtggactctg	tgaaggcccg	attcaccatc	tccagagaca	acggcaagaa	ctcactgtat	240
ctgcaaatga	acagectgag	agccgaggac	acggctgtgt	attactgtgt	gagagatcga	300
ggtatagaag	tggctggccc	ctttgactac	tggggccagg	gaacctgtgt	caccgtctcc	360
tca						363

<210> SEQ ID NO 310
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 310

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Ley	Val	Gln	Pro	Gly	Gly	
1							5		10			15			
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Lys	Tyr
	20						25				30				

-continued

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Asn Ile Lys Glu Asp Gly Asn Glu Lys Tyr Tyr Val Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Val Arg Asp Arg Gly Ile Glu Val Ala Gly Pro Phe Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 311

<211> LENGTH: 319

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 311

gacatccaga tgaccaggc tccttccacc ctgtctgcatt ctgttaggaga cagagtacc 60
 atcaacttgcc gggcccgatca gactattatt aattgggtgg cctggtatca gcagaaacca 120
 gggaaagccc ctaagctctt gatctataag gcgtctagtt tagaaagtgg ggtcccatca 180
 aggttcagcg gcagtggtatc tgggacagaa ttcaactctca ccatcagcag cctgcagcct 240
 gatgattttt caacttatta ctgccaacag tataataggt attggacgtt cggccaaggg 300
 accaagggtgg aaatcaaac 319

<210> SEQ ID NO 312

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 312

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Thr Ile Ile Asn Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Arg Tyr Trp Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 313

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 313

```
caggtgcagc tggtgaggc tgggggaggc gtggtccagc ctggggaggc cctgagactc      60
tcctgtgcag cgtctggatt cacttca gactatggca tgcactgggt ccgcaggct      120
ccaggcaagg ggctggagtg ggtggcagtt atatggatg atgaatttaa taaatactat      180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat      240
ctgcaaata gacagectgag agccgaggac acggctgtgtt attactgtgc gagagagaga      300
gagagtggat acagttatgg ttttactac tggggccagg gaaccctggt caccgtctcc      360
tca                                              363
```

<210> SEQ ID NO 314

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 314

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1							5		10					15	

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
	20							25					30		

Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35							40				45			

Ala	Val	Ile	Trp	Tyr	Asp	Glu	Phe	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50						55					60			

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65							70			75			80		

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
	85							90					95		

Ala	Arg	Glu	Arg	Glu	Ser	Gly	Tyr	Ser	Tyr	Gly	Phe	Asp	Tyr	Trp	Gly
	100							105				110			

Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
	115						120	

<210> SEQ ID NO 315

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 315

ggattcacct tcagtagcta tgcc 24

<210> SEQ ID NO 316

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 316

Gly	Phe	Thr	Phe	Ser	Ser	Tyr	Gly
1						5	

<210> SEQ ID NO 317

<211> LENGTH: 24

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 317

atatggtagt atgaatttaa taaa

24

<210> SEQ ID NO 318
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 318

Ile Trp Tyr Asp Glu Phe Asn Lys
1 5

<210> SEQ ID NO 319
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 319

gcgagagaga gagagagtgg atacagttat ggaaaaact ac

42

<210> SEQ ID NO 320
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 320

Ala Arg Glu Arg Glu Ser Gly Tyr Ser Tyr Gly Phe Asp Tyr
1 5 10

<210> SEQ ID NO 321
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 321

gaaatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccaggggaa aagagccacc 60
ctctcctgca gggccggtaa gagtgtagc agcaacttag cctggtagca gcaaaaacct 120
ggccaggctc ccaggctcct catctatggt gcgtccacca gggccactgg tatcccagcc 180
aggttcagtg gcagtggttc tgggacagag ttcactctca ccatcagcag cctgcagtct 240
gaagattttg cagtttatta ctgtcagcag tataataact ggtggacgtt cggccaaggg 300
accaagggtgg aaatcaaa 318

<210> SEQ ID NO 322
<211> LENGTH: 106
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 322

US 9,402,898 B2

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Glu	Ile	Val	Met	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
1					5				10					15	

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Gly	Gln	Ser	Val	Ser	Ser	Asn
	20					25							30		

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
	35					40					45				

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
	50				55				60						

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
65					70			75					80		

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Asn	Trp	Trp	Thr
					85			90					95		

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys						
					100				105						

<210> SEQ ID NO 323
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 323

cagagtgtta gcagcaac

18

<210> SEQ ID NO 324
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 324

Gln Ser Val Ser Ser Asn
1 5

<210> SEQ ID NO 325
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 325

ggtgcggtcc

9

<210> SEQ ID NO 326
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 326

Gly Ala Ser
1

<210> SEQ ID NO 327
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 327

```
cagcagtata ataactggtg gacg
<210> SEQ ID NO 328
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 328

Gln	Gln	Tyr	Asn	Asn	Trp	Trp	Thr
1					5		

```
<210> SEQ ID NO 329
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 329

cagggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggagggt cctgagactc	60
tccctgtgcag cgtctggatt caccttcagt agctatggca tgcactgggt ccgccaggct	120
ccaggccaagg ggcttggagtg ggtggcagtt atatggatgt atgaatttaa taaatactat	180
gcagactccg tgaaggggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgc当地atga acagecctgag agccgaggac acggctgtgt attactgtgc gagagagaga	300
gagagtggat acagttatgg ttttactac tggggccagg gaacccttgtt caccgtctcc	360
tca	363

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<210> SEQ ID NO 330
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 330

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1				5			10				15				

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
			20				25			30					

Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40				45						

Ala	Val	Ile	Trp	Tyr	Asp	Glu	Phe	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50				55			60							

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65				70			75		80						

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
		85				90				95					

Ala	Arg	Glu	Arg	Glu	Ser	Gly	Tyr	Ser	Tyr	Gly	Phe	Asp	Tyr	Trp	Gly
	100				105				110						

Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
	115				120			

<210> SEQ ID NO 331

<211> LENGTH: 318

<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 331

gaaaatagtga	tgacgcagtc	tccagccacc	ctgtctgtgt	ctccaggggaa	aagagccacc	60
ctctcctgca	gggcgggtca	gagtgtttagc	agcaacttag	cctggtagcca	gcaaaaacct	120
ggccaggctc	ccaggctcct	catctatggt	gegtccacca	gggccactgg	tatcccagcc	180
aggttcagtg	gcagtggtc	tgggacagag	ttcactctca	ccatcagcag	cctgcagtt	240
gaagatttg	cagtttatta	ctgtcagcag	tataataact	ggtggacgtt	cggccaaggg	300
accaagggtgg	aaatcaaa					318

<210> SEQ_ID NO 332

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 332

Glu	Ile	Val	Met	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
1				5					10						15

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Gly	Gln	Ser	Val	Ser	Ser	Asn
	20					25									30

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
		35				40						45			

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
	50				55							60			

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
65				70				75							80

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Asn	Trp	Trp	Thr
		85					90								95

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys						
				100					105						

<210> SEQ_ID NO 333

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 333

cagggtgcagc	tggggaggc	tggggaggc	gtgggtccagc	ctggggaggc	cctgagactc	60
tccctgtcgag	cgtctggatt	cacttcagt	agctatggca	tgcactgggt	ccggccaggct	120
ccaggcaagg	ggctggaggc	ggctggaggc	atatggat	atggat	atggat	180
gcagactccg	tgaaggggccg	attcaccatc	tccagagaca	actccaagaa	cacgctgtat	240
ctgc当地atga	acagcctgag	agccgaggac	acggctgtgt	attactgtgc	gagagagaga	300
gagagtgat	acagttatgg	ttttgactac	tggggccagg	gaaccctgg	caccgtctcc	360
tca						363

<210> SEQ_ID NO 334

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 334

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1				5			10				15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
	20				25					30					

Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40					45					

Ala	Val	Ile	Trp	Tyr	Asp	Glu	Phe	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val
	50				55			60							

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
	65				70			75			80				

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
	85				90					95					

Ala	Arg	Glu	Arg	Glu	Ser	Gly	Tyr	Ser	Tyr	Gly	Phe	Asp	Tyr	Trp	Gly
	100				105					110					

Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
	115				120			

<210> SEQ ID NO 335

<211> LENGTH: 319

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 335

gaaaatagtga	tgacgcagtc	tccagccacc	ctgtctgtgt	ctccaggggaa	aagagccacc	60
ctctcctgca	gggccagtc	gaggttgtac	agcaacttag	cctggcacca	gcagaaacct	120
ggccaggctc	ccaggctcct	catctatggt	gcgtccacca	gggccactgg	tatcccagcc	180
aggttcagtg	gcagtgggtc	tggcacagag	ttcaactctca	ccatcagcag	cctgcagtc	240
gaagattttg	cagtttatta	ctgtcagcag	tataataact	ggtggacggtt	cggccaaggg	300
accaagggtgg	aaatcaaac					319

<210> SEQ ID NO 336

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 336

Glu	Ile	Val	Met	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Val	Ser	Pro	Gly
1				5				10			15				

Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Asn
	20				25					30					

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Ile
	35			40						45				

Tyr	Gly	Ala	Ser	Thr	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly
	50				55			60							

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Ser
	65				70			75		80					

Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Asn	Trp	Trp	Thr
	85				90					95					

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

-continued

100 105

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<210> SEQ ID NO 337
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 337

caggttcagc tggcgactc tggacctgag gtgaaggagc ctggggcctc agtgaaggc 60
tcctgcagg cttctggta caccttacc acctatacgta tcacctgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaattatga cacaattat 180
gcacagaaga tccaggcag agtccccatc accacagaca catccacgaa cacagcctac 240
atggaaactga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggcgat 300
ttctggatta attattccta ctactactac ggtgtggacg tctggggcca agggaccacg 360
gtcacccgtct cctca 375

```

```

<210> SEQ ID NO 338
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 338

Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Glu Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30

Ser Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Tyr Asp Thr Asn Tyr Ala Gln Lys Ile
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asp Phe Trp Ile Asn Tyr Ser Tyr Tyr Tyr Gly Val
100 105 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

```

```

<210> SEQ ID NO 339
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 339

ggttacacct ttaccaccta tagt 24

```

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<210> SEQ ID NO 340
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

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-continued

<400> SEQUENCE: 340

Gly Tyr Thr Phe Thr Thr Tyr Ser
1 5

<210> SEQ ID NO 341

<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 341

atcagcgctt acaattatga caca

24

<210> SEQ ID NO 342

<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 342

Ile Ser Ala Tyr Asn Tyr Asp Thr
1 5

<210> SEQ ID NO 343

<211> LENGTH: 54
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 343

gcgagaggcg atttctggat taattattcc tactactact acgggtgtgga cgtc

54

<210> SEQ ID NO 344

<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 344

Ala Arg Gly Asp Phe Trp Ile Asn Tyr Ser Tyr Tyr Tyr Gly Val
1 5 10 15

Asp Val

<210> SEQ ID NO 345

<211> LENGTH: 339
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 345

gacattgtga tgacgcagtc tccactctcc ctgccccgtca tccctggaga gcccggctcc 60

atctccttgca ggtcttagtca gagcctccctg catagtaatg gataacaacta tttggatgg 120

tacctgcaga agccaggggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacagggtt cagtggcagt ggatcaggca cagatttac actgaaaatc 240

agcagagtggtt aggctgagga tgttgggtt tattactgca tgcaagctct acaaaactccc 300

atgtacactt ttggccaggg gaccaagctg gagatcaa 339

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<210> SEQ_ID NO 346
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 346

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Ile	Pro	Gly
1															15
Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser
															30
Asn	Gly	Tyr	Asn	Tyr	Leu	Asp	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
															45
Pro	Gln	Leu	Leu	Ile	Tyr	Leu	Gly	Ser	Asn	Arg	Ala	Ser	Gly	Val	Pro
															60
Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Lys	Ile
65															80
Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys	Met	Gln	Ala
															95
Leu	Gln	Thr	Pro	Met	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile
															110
100															

Lys

<210> SEQ_ID NO 347
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 347

cag	agc	tcc	tgc	atg	taa	tgg	ata	aca	ac	tat						33
-----	-----	-----	-----	-----	-----	-----	-----	-----	----	-----	--	--	--	--	--	----

<210> SEQ_ID NO 348
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 348

Gln	Ser	Leu	Leu	His	Ser	Asn	Gly	Tyr	Asn	Tyr					
1															10

<210> SEQ_ID NO 349
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 349

ttgggttct

9

<210> SEQ_ID NO 350
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 350

Leu Gly Ser
1<210> SEQ ID NO 351
<211> LENGTH: 30
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 351

atgcaagctc tacaaaactcc catgtacact 30

<210> SEQ ID NO 352
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 352

Met Gln Ala Leu Gln Thr Pro Met Tyr Thr
1 5 10<210> SEQ ID NO 353
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 353

cagggttcagc tgggtgcagtc tggacctgag gtgaaggagc ctggggcctc agtgaaggc 60
tcctgcagg cttctggta caccttacc acctatagta tcacctgggt gcgacaggcc 120
cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaaattatga cacaatttat 180
gcacagaaga tccagggcag agtcaccatg accacagaca catccacgaa cacagctac 240
atggaaactga ggagcctgag atctgacgc acggccgtgt attactgtgc gagaggcgat 300
ttctggatta attattccta ctactactac ggtgtggacg tctggggcca agggaccacg 360
gtcacccgtct cc 372<210> SEQ ID NO 354
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 354

Gln Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Glu Pro Gly Ala
1 5 10 15Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30Ser Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45Gly Trp Ile Ser Ala Tyr Asn Tyr Asp Thr Asn Tyr Ala Gln Lys Ile
50 55 60Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Asn Thr Ala Tyr
65 70 75 80

-continued

Met	Glu	Leu	Arg	Ser	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
85								90							95

Ala	Arg	Gly	Asp	Phe	Trp	Ile	Asn	Tyr	Ser	Tyr	Tyr	Tyr	Tyr	Gly	Val
100								105							110

Asp	Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser
115								120			

<210> SEQ ID NO 355

<211> LENGTH: 339

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 355

gatattgtga	tgactcagtc	tccactctcc	ctgccccgtca	tccctggaga	gccggccctcc	60
atctcctgca	ggtcttagtca	gagccctcctg	catacataatg	gataacaacta	tttggatgg	120
tacctgcaga	agccaggggca	gtctccacag	ctcctgtatct	atttgggttc	taatcgccc	180
tccggggtcc	ctgacaggtt	cagtggcagt	ggatcaggca	cagatttac	actgaaaatc	240
agcagagtg	aggctgagga	tgttgggtt	tattactgca	tgcaagctct	acaaactccc	300
atgtacactt	ttggccaggg	gaccaagctg	gagatcaaa			339

<210> SEQ ID NO 356

<211> LENGTH: 113

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 356

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Ile	Pro	Gly
1								5				10		15	

Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser
20								25				30			

Asn	Gly	Tyr	Asn	Tyr	Leu	Asp	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
35								40				45			

Pro	Gln	Leu	Leu	Ile	Tyr	Leu	Gly	Ser	Asn	Arg	Ala	Ser	Gly	Val	Pro
50								55				60			

Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Lys	Ile
65								70				75			80

Ser	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys	Met	Gln	Ala
85								90				95			

Leu	Gln	Thr	Pro	Met	Tyr	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile
100								105				110			

Lys

<210> SEQ ID NO 357

<211> LENGTH: 373

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 357

caggttcagc	tggtgcagtc	tggagctgag	gtgaagaagc	ctggggccctc	agtgaaggtc	60
tcctgcagg	cttctggta	cacctttacc	acctatactt	tcaagctgggt	gcgcacaggcc	120
cctggacaag	ggcttgagtg	gatggatgg	atcagcgctt	acaattatga	cacaaactat	180

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gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagccctac      240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggcgat      300
ttctggatta attattccta ctactactac ggtgtggacg tctggggcca agggaccacg      360
gtcaccgtct cct                                         373

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<210> SEQ ID NO 358
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 358

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1           5           10          15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20          25          30

Ser Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35          40          45

Gly Trp Ile Ser Ala Tyr Asn Tyr Asp Thr Asn Tyr Ala Gln Lys Leu
50          55          60

Gln Gly Arg Val Thr Met Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Gly Asp Phe Trp Ile Asn Tyr Ser Tyr Tyr Tyr Gly Val
100         105         110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
115         120

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<210> SEQ ID NO 359
<211> LENGTH: 340
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 359

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggccctcc      60
atctcctgcg ggtcttagtca gagecctctg catagtaatg gataacaacta tttggatgg      120
tacctgcaga agccagggca gtctccacag ctccctgatct atttgggttc taatcgggcc      180
tccggggtcc ctgacagggtt cagtggcagt ggatcaggca cagatttac actgaaaatc      240
agcagagttt aggctgagga tggtgggtt tattactgca tgcaagctct acaaactccc      300
atgtacactt ttggccaggg gaccaagctg gagatcaaac                               340

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<210> SEQ ID NO 360
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 360

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1           5           10          15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser

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219**220**

-continued

20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95

Leu Gln Thr Pro Met Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
 100 105 110

Lys

<210> SEQ ID NO 361

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 361

gaggtgcagc tggtgagtc tgggggaggc ttggtccagc ctggggggtc cctgagactc	60
tccctgtcgac cctctggatt cgcctttaga agttattggta tgacctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggtggccaac atacagcaag atggaaatga taaatactat	180
gtggactctgt tgaaggcccg attcaccatc tccagagaca acgccaagaa ctcactgttat	240
ctgcaaatga acagectgag agccgaggac acggctgtgt attactgtgc gagagatacc	300
ggtatagcag aagctggtcc ttttactac tggggccagg gaaccctggt caccgtctcc	360
tca	363

<210> SEQ ID NO 362

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 362

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly	
1 5 10 15	

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Arg Ser Tyr	
20 25 30	

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
35 40 45	

Ala Asn Ile Gln Gln Asp Gly Asn Asp Lys Tyr Tyr Val Asp Ser Val	
50 55 60	

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr	
65 70 75 80	

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	

Ala Arg Asp Thr Gly Ile Ala Glu Ala Gly Pro Phe Asp Tyr Trp Gly	
100 105 110	

Gln Gly Thr Leu Val Thr Val Ser Ser	
115 120	

<210> SEQ ID NO 363

221**222**

-continued

<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 363

ggattcgct ttagaagttt ttgg

24

<210> SEQ ID NO 364
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 364

Gly Phe Ala Phe Arg Ser Tyr Trp
1 5

<210> SEQ ID NO 365
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 365

atacagcaag atggaaatga taaa

24

<210> SEQ ID NO 366
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 366

Ile Gln Gln Asp Gly Asn Asp Lys
1 5

<210> SEQ ID NO 367
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 367

gcgagagata ccggatatacgc agaagctggt ccttttgact ac

42

<210> SEQ ID NO 368
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 368

Ala Arg Asp Thr Gly Ile Ala Glu Ala Gly Pro Phe Asp Tyr
1 5 10

<210> SEQ ID NO 369
<211> LENGTH: 318
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 369

gacatccaga	tgaccaggc	tccttccacc	ctgtctgcat	ctgttaggaga	cagagtctcc	60
atcaacttgcc	gggcaggta	gactattatt	agctgggtgg	cctggtatca	gcagaaacca	120
ggaaaagccc	ctaggctcct	gatctataag	gctgtctatgt	tagaaagtgg	ggtccccatca	180
aggttcagcg	gcagtggtac	tgggacagaa	ttcactctca	ccatcaacag	cctgcagcct	240
gatgatttg	caacttatta	ctgccaacag	tataatcggt	attggacgtt	cggccaaggg	300
accaagggtgg	aaatcaaa					318

<210> SEQ ID NO 370

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 370

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1							5		10					15	

Asp	Arg	Val	Ser	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Thr	Ile	Ile	Ser	Trp
							20		25				30		

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Arg	Leu	Leu	Ile
						35		40			45				

Tyr	Lys	Ala	Ser	Ser	Leu	Glu	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55				60					

Ser	Gly	Ser	Gly	Thr	Glu	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Gln	Pro
65					70				75				80		

Asp	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn	Arg	Tyr	Trp	Thr
						85		90			95				

Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys						
					100				105						

<210> SEQ ID NO 371

<211> LENGTH: 18

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 371

cagacttatta	ttagctgg		18
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<210> SEQ ID NO 372

<211> LENGTH: 6

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 372

Gln	Thr	Ile	Ile	Ser	Trp										
1					5										

<210> SEQ ID NO 373

<211> LENGTH: 9

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 373

aaggcgtct

9

<210> SEQ ID NO 374
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 374

Lys Ala Ser
1

<210> SEQ ID NO 375
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 375

caacagttata atcgatttg gacg

24

<210> SEQ ID NO 376
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 376

Gln Gln Tyr Asn Arg Tyr Trp Thr
1 5

<210> SEQ ID NO 377
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 377

gaggtgcagc tgggggagtc tgggggagtc ttgggtccagc ctggggggtc cctgagactc	60
tccctgtcgac cctctggatt cgcctttaga agttattggta tgacctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggtggccaac atacagcaag atggaaatga taaatactat	180
gtggactctg tgaaggccc attaccatc tccagagaca acgccaagaa ctcactgtat	240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatacc	300
ggtatagcag aagctggtcc ttttactac tggggccagg gaaccctggt caccgtctcc	360
tca	363

<210> SEQ ID NO 378
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 378

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

-continued

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Arg Ser Tyr
 20 25 30

Trp Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Asn Ile Gln Gln Asp Gly Asn Asp Lys Tyr Tyr Val Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Asp Thr Gly Ile Ala Glu Ala Gly Pro Phe Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 379

<211> LENGTH: 318

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 379

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctgttaggaga cagagtctcc 60

atcacttgcc gggccagtc gactattatt agctggttgg cctggtatca gcagaaacca 120

gggaaagccc ctaggctcct gatctataag gcgtctagtt tagaaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tggcacagaa ttcactctca ccatcaacag cctgcagcct 240

gatgattttg caacttatta ctgccaacag tataatcggtt attggacgtt cggccaaggg 300

accaagggtgg aaatcaaa 318

<210> SEQ ID NO 380

<211> LENGTH: 106

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 380

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Thr Ile Ile Ser Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
 35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
 65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Arg Tyr Trp Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 381

<211> LENGTH: 363

<212> TYPE: DNA

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229**230**

-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 381

gagggtgcagc	tgggtggagtc	tgggggaggc	ttgggtccagc	cgggggggtc	cctgagactc	60
tccctgtcgag	cctctggatt	cgcctttaga	agttatttgg	tgagctgggt	ccgccaggct	120
ccagggaaagg	ggctggagtg	ggtgtggcaac	atacagcaag	atggaaatga	taaatactat	180
gtggactctg	tgaaggggccg	attcaccatc	tccagagaca	acgccaagaa	ctcactgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggctgtgt	attactgtgc	gagagatacc	300
ggtatagcag	aagctggtcc	ttttgactac	tggggccagg	gaaccctgg	caccgtctcc	360
tca						363

<210> SEQ ID NO 382

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 382

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly
1															
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Ala	Phe	Arg	Ser	Tyr
Trp	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
Ala	Asn	Ile	Gln	Gln	Asp	Gly	Asn	Asp	Lys	Tyr	Tyr	Val	Asp	Ser	Val
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Ser	Leu	Tyr
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
Ala	Arg	Asp	Thr	Gly	Ile	Ala	Glu	Ala	Gly	Pro	Phe	Asp	Tyr	Trp	Gly
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser							

<210> SEQ ID NO 383

<211> LENGTH: 319

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 383

gacatccaga	tgacccagtc	tccttccacc	ctgtctgcat	ctgttaggaga	cagagtccacc	60
atcacttgc	ggcccaagtca	gacttatttt	agctgggtgg	cctggtatca	gcagaaaacca	120
ggaaaaagccc	ctaagctcct	gatctataag	gcgtcttagt	tagaaagtgg	ggtccccatca	180
aggttcagcg	gcagtggtatc	tgggacagaaa	ttcactctca	ccatcagcag	cctgcagcct	240
atgtatgg	caacttatta	ctgccaacag	tataatcggtt	attggacggtt	cggccaagg	300
accaagggtgg	aaatcaaac					319

<210> SEQ ID NO 384

<211> LENGTH: 106

-continued

<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 384

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Thr	Leu	Ser	Ala	Ser	Val	Gly
1			5			10				15					

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Thr Ile Ile Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Arg Tyr Trp Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ_ID NO 385
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 385

gacgtgcaac	tgtggagtc	tggggagac	ttggtagc	ctgggggtc	cctgagactc	60
tccgtgtt	aatcgatt	cacctttaga	aactatgtca	tgtatctgggt	ccggcaggct	120
ccagggaaagg	ggctggagt	ggtctcagg	attagtaata	gtggtggtac	tacacactac	180
acagactccg	tgaaggccg	gttccaccatt	tccagagaca	attccaaaaaa	cacgctgtat	240
ctgcaaatta	acagtctgcg	agccgaggat	acggccgtct	attactgtgc	gaaggctac	300
ttagacacat	ctctgattga	ggggactgg	ttcgaccct	ggggccaggg	aaccctggc	360
accgtctcct	ca					372

<210> SEQ_ID NO 386
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 386

Asp	Val	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Asp	Leu	Val	Gln	Pro	Gly	Gly
1				5			10		15						

Ser Leu Arg Leu Ser Cys Glu Ala Ser Gly Phe Thr Phe Arg Asn Tyr
20 25 30

Val Met Ile Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Asn Ser Gly Gly Thr Thr His Tyr Thr Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Ile Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

-continued

Ala Lys Gly Tyr Leu Asp Thr Ser Leu Ile Glu Gly Asn Trp Phe Asp
 100 105 110

Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 387
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 387

ggattcacct ttagaaacta tgtc 24

<210> SEQ ID NO 388
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 388

Gly Phe Thr Phe Arg Asn Tyr Val
 1 5

<210> SEQ ID NO 389
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 389

attagtaata gtgggtggtac taca 24

<210> SEQ ID NO 390
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 390

Ile Ser Asn Ser Gly Gly Thr Thr
 1 5

<210> SEQ ID NO 391
<211> LENGTH: 51
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 391

gcgaagggct acttagacac atctctgatt gaggggaact ggttcgaccc c 51

<210> SEQ ID NO 392
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 392

-continued

Ala	Lys	Gly	Tyr	Leu	Asp	Thr	Ser	Leu	Ile	Glu	Gly	Asn	Trp	Phe	Asp
1				5				10					15		

Pro

<210> SEQ ID NO 393
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 393

aatattgtga	tgactcagtc	tccactctcc	ctgcccgtca	cccctggaga	gccggcctcc	60
atctcctgca	ggtctagtca	gagcctccta	catacgtaatg	gattcaacta	tttgaattgg	120
ttcctgcaga	agccaggggca	gtctccacag	ctcctgatct	atttgggttc	taatcgggcc	180
tccggggtcc	ctgacaagtt	cagtggcagt	ggatcaggca	cagatttac	actgaacatc	240
aacagagtg	aggctgagga	tgttggatt	tatttctgca	tgcagactct	acaaaactccc	300
ctcacttcg	gcggaggggac	caaggtggag	atcaaa			336

<210> SEQ ID NO 394
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 394

Asn	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly
1				5				10				15			

Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser
				20				25				30			

Asn	Gly	Phe	Asn	Tyr	Leu	Asn	Trp	Phe	Leu	Gln	Lys	Pro	Gly	Gln	Ser
					35			40			45				

Pro	Gln	Leu	Leu	Ile	Tyr	Leu	Gly	Ser	Asn	Arg	Ala	Ser	Gly	Val	Pro
					50			55			60				

Asp	Lys	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile
					65			70			75			80	

Asn	Arg	Val	Glu	Ala	Glu	Asp	Val	Gly	Ile	Tyr	Phe	Cys	Met	Gln	Thr
					85			90			95				

Leu	Gln	Thr	Pro	Leu	Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys
					100			105			110			

<210> SEQ ID NO 395
<211> LENGTH: 33
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 395

cagagcctcc tacatagtaa tggattcaac tat 33

<210> SEQ ID NO 396
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 396

-continued

Gln Ser Leu Leu His Ser Asn Gly Phe Asn Tyr
1 5 10

```
<210> SEQ ID NO 397
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 397

9

<210> SEQ ID NO 398

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<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 398

Leu Gly Ser
1

```
<210> SEQ ID NO 399
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 399

atqcaqactc tacaaactcc cctcact

27

```
<210> SEQ ID NO 400
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 400

Met Gln Thr Leu Gln Thr Pro Leu Thr
1 5

```
<210> SEQ ID NO 401
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 401

gaggtgcgc	tgttgaggc	tggggagac	tttgtacagc	ctgggggtc	cctgagactc	60
tcctgtgaag	cctctggatt	cacctttaga	aactatgtca	tgtatctgggt	ccgcaggct	120
ccagggaaagg	ggctggagt	ggtctcagg	attagtaata	gtgggtgtac	tacacactac	180
acagactccg	tgaagggccg	gttcaccatt	tccagagaca	attccaaaaa	cacgtgtat	240
ctgcaaatta	acagtctgcg	agccgaggat	acggccgtct	attachtgtc	gaaggggctac	300
ttagacacat	ctctgattga	ggggactgg	ttcgaccct	ggggccagg	aacctgtgtc	360
accgtctcc	ca					372

-continued

<210> SEQ_ID NO 402
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 402

Glu	Val	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Asp	Leu	Val	Gln	Pro	Gly	Gly
1					5				10				15		

Ser	Leu	Arg	Leu	Ser	Cys	Glu	Ala	Ser	Gly	Phe	Thr	Phe	Arg	Asn	Tyr
	20				25					30					

Val	Met	Ile	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
	35				40					45					

Ser	Gly	Ile	Ser	Asn	Ser	Gly	Gly	Thr	Thr	His	Tyr	Thr	Asp	Ser	Val
	50				55					60					

Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
	65				70				75				80		

Leu	Gln	Ile	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
	85				90				95						

Ala	Lys	Gly	Tyr	Leu	Asp	Thr	Ser	Leu	Ile	Glu	Gly	Asn	Trp	Phe	Asp
	100				105					110					

Pro	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser				
	115				120										

<210> SEQ_ID NO 403
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 403

gatattgtga	tgactcagtc	tccactctcc	ctgccccgtca	cccctggaga	gccgggcctcc	60
atctccctgca	ggtcttagtca	gagccctcta	catacataatg	gattcaacta	tttgaatgg	120
ttcctgtcaga	agccaggggca	gtctccacag	ctcctgtatct	atttgggttc	taatcgcc	180
tccgggggtcc	ctgacaagtt	cagtggcagt	ggatcaggca	cagatttac	actgaacatc	240
aacagagttgg	aggctgagga	tgttggaaatt	tatttctgca	tgcagactct	acaaaactccc	300
ctcactttcg	gcggaggac	caaggtggag	atcaaa			336

<210> SEQ_ID NO 404
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 404

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Leu	Ser	Leu	Pro	Val	Thr	Pro	Gly
1					5				10			15			

Glu	Pro	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser
	20					25						30			

Asn	Gly	Phe	Asn	Tyr	Leu	Asn	Trp	Phe	Leu	Gln	Lys	Pro	Gly	Gln	Ser
	35				40					45					

Pro	Gln	Leu	Leu	Ile	Tyr	Leu	Gly	Ser	Asn	Arg	Ala	Ser	Gly	Val	Pro
	50				55					60					

Asp	Lys	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile
	65				70				75				80		

-continued

Asn Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Phe Cys Met Gln Thr
 85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> SEQ ID NO 405

<211> LENGTH: 372

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 405

gagggtgcagc tgggggagtc ttgggtacagc ctggggggtc cctgagactc	60
tccctgtcgag octctggatt cacctttaga aactatgtca tgagctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggtctcgatc attagtaata gtgggtgtac tacataactac	180
gcagactccg tgaaggcccg gttcaccatc tccagagaca attccaagaa cacgctgttat	240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaagggtac	300
ttagacacat ctctgattga ggggaactgg ttgcacccct gggggcaggg aaccctggtc	360
accgtctcct ca	372

<210> SEQ ID NO 406

<211> LENGTH: 124

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 406

Glu Val Gln Leu Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly	
1 5 10 15	

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asn Tyr	
20 25 30	

Val Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
35 40 45	

Ser Ala Ile Ser Asn Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val	
50 55 60	

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr	
65 70 75 80	

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	

Ala Lys Gly Tyr Leu Asp Thr Ser Leu Ile Glu Gly Asn Trp Phe Asp	
100 105 110	

Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser	
115 120	

<210> SEQ ID NO 407

<211> LENGTH: 337

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 407

gatattgtga tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggccctcc	60
--	----

atctcctgca ggtctagtca gagcctccta catagtaatg gattcaacta tttggatgg	120
--	-----

-continued

tacctgcaga agccaggcgtctccacag ctctgtatctttgggttc taatcgcc 180
tccgggttcc ctgacagggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
aggcagactgg aggctgagga tttgggttattactgca tgcagactct acaaactccc 300
ctcaactttcg qcggqaggac caagggtggat atcaaac 337

```

<210> SEQ ID NO 408
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 408

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Phe Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Thr
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

```

```
<210> SEQ ID NO 409
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 409

gagggtgcagc tggggggggc ttgggtacagc ctggggggtc cctgagactc      60
tccctgtgcag cctctggatt cacctttagg aagtatgeca tgagctgggt ccgcaggct    120
ccagggaaagg ggctggaggc ggtctcgat attagtgtta gtgggtgtaa cacatactac    180
gcagactccg tgaaggcccg gttcaccatc tccagagaca attccaagaa cacgtgtat    240
ctgcactatg acagcctgag agccgaggac acggccgtat attachgtgc gaaggatcta    300
acggatattg tacttatggt gtatgtcgac tactggggcc agggaaacctt ggtcaccgtc    360
tcctcta                                         366
```

```
<210> SEQ ID NO 410
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 410

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1           5           10          15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Lys Tyr
20          25          30
```

-continued

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Val Ser Gly Gly Asn Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Leu Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Leu Thr Asp Ile Val Leu Met Val Tyr Val Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ_ID NO 411

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 411

ggattcacct ttaggaagta tgcc

24

<210> SEQ_ID NO 412

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 412

Gly Phe Thr Phe Arg Lys Tyr Ala
1 5

<210> SEQ_ID NO 413

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 413

attagtgttta gtgggtgtaa caca

24

<210> SEQ_ID NO 414

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 414

Ile Ser Val Ser Gly Gly Asn Thr
1 5

<210> SEQ_ID NO 415

<211> LENGTH: 45

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 415

gcgaaggatc taacggatat tgtactttatg gtgttatgtcg actac

45

-continued

<210> SEQ_ID NO 416
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 416

Ala	Lys	Asp	Leu	Thr	Asp	Ile	Val	Leu	Met	Val	Tyr	Val	Asp	Tyr
1														
													15	

<210> SEQ_ID NO 417
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 417

gacatccaga	tgaccaggc	tccatcttcc	gtgtctgcat	ctgttaggaga	cagagtccacc	60
atcacttgtc	gggcgagtca	ggatattgac	aggtggtag	cctggtatca	gcagaaacca	120
gggaaagccc	ctaagctcct	gatctatgt	gcatccagtt	tgcaaagtgg	ggtccccatca	180
aggttcagcg	gcagtggtac	tgggacagat	ttcactctca	ccatcagcac	cctgcagcct	240
gaagattttg	caacttacta	ttgtcaacag	gctaacagtt	tgccgttcac	tttcggcgga	300
gggaccaagg	tggagatcaa	a				321

<210> SEQ_ID NO 418
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 418

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Val	Ser	Ala	Ser	Val	Gly
1															
														15	

Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Asp	Ile	Asp	Arg	Trp
20															
														30	

Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile
35															
														45	

Tyr	Ala	Ala	Ser	Ser	Leu	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
50															
														60	

Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Thr	Leu	Gln	Pro
65															
														80	

Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ala	Asn	Ser	Leu	Pro	Phe
85															
														95	

Thr	Phe	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys						
100															
														105	

<210> SEQ_ID NO 419
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 419

caggatattg acaggtgg

-continued

<210> SEQ ID NO 420
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 420

Gln Asp Ile Asp Arg Trp
1 5

<210> SEQ ID NO 421
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 421

gctgcatcc

9

<210> SEQ ID NO 422
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 422

Ala Ala Ser
1

<210> SEQ ID NO 423
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 423

caaacaggcta acagtttgcc gttcact

27

<210> SEQ ID NO 424
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 424

Gln Gln Ala Asn Ser Leu Pro Phe Thr
1 5

<210> SEQ ID NO 425
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 425

gaggtgcagc tgttggagtctggggaggc ttggtagcagc ctggggggtc cctgagactc 60

tccctgtcagc cctctggatt cacctttagg aagtatgccatgactc tgagctgggt ccgccaggct 120

ccagggaaagg ggctggagtggctcagtt attagtgtta gtgggtggtaa cacatactac 180

251**252**

-continued

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaactga acagecctgag agccgaggac acggccgtat attactgtgc gaaggatcta	300
acggatattg tacttatggt gtatgtcgac tactggggcc agggAACCTT ggtcaccgtc	360
tcctca	366

<210> SEQ ID NO 426
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 426

Glu Val Gln Leu Leu Glu Ser Gly Gly			
1	5	10	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Lys Tyr			
20	25	30	
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
35	40	45	
Ser Val Ile Ser Val Ser Gly Gly Asn Thr Tyr Tyr Ala Asp Ser Val			
50	55	60	
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr			
65	70	75	80
Leu Gln Leu Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	
Ala Lys Asp Leu Thr Asp Ile Val Leu Met Val Tyr Val Asp Tyr Trp			
100	105	110	
Gly Gln Gly Thr Leu Val Thr Val Ser Ser			
115	120		

<210> SEQ ID NO 427
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 427

gacatccaga tgaccttgtc tccatcttcc gtgtctgcat ctgttaggaga cagagtacc	60
atcacttgta gggcgagtca ggatattgac aggtggtag cctggatca gcagaaacca	120
ggaaaagccc ctaagctcct gatctatgtc gcatccagg tgcaaagtgg ggtccatca	180
aggttcagcg gcagtggatc tggacagat ttcaactctca ccatcagcac cctgcagcct	240
gaagatTTT caacttacta ttgtcaacag gctaacagg tgccgttac tttcgccga	300
gggaccaagg tggagatcaa a	321

<210> SEQ ID NO 428
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 428

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly			
1	5	10	15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Asp Arg Trp			
20	25	30	

-continued

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Thr Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Leu Pro Phe
 85 90 95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> SEQ ID NO 429
 <211> LENGTH: 366
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 429

gaggtgcagc	tgttgaggc	tgggggaggc	ttggtagacgc	ctggggggtc	cctgagactc	60
tcctgtgcag	cctctggatt	cacctttagg	aagtatgcca	tgagctgggt	ccgccaggct	120
ccagggaaagg	ggctggaggc	ggctctcagct	attagtgtta	gtggtggtaa	cacatactac	180
gcagactccg	tgaaggggccg	gttcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggccgtat	attactgtgc	gaaggatcta	300
acggatattg	tacttatggt	gtatgtcgac	tactggggcc	agggAACCT	ggtcaccgtc	360
tcctca						366

<210> SEQ ID NO 430
 <211> LENGTH: 122
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 430

Glu Val Gln	Leu Leu Glu	Ser Gly	Gly	Ley Val	Gln Pro	Gly Gly
1	5	10	15			
Ser Ley Arg	Leu Ser Cys	Ala Ala Ser	Gly Phe	Thr Phe	Arg Lys	Tyr
20	25			30		
Ala Met Ser	Trp Val Arg	Gln Ala Pro	Gly Lys	Gly Ley	Glu Trp	Val
35	40	45				
Ser Ala Ile	Ser Val Ser	Gly Gly	Asn Thr	Tyr Tyr	Ala Asp	Ser Val
50	55	60				
Lys Gly Arg	Phe Thr Ile	Ser Arg Asp	Asn Ser	Lys Asn	Thr Ley	Tyr
65	70	75	80			
Ley Gln Met	Asn Ser Ley Arg	Ala Glu Asp	Thr Ala Val	Tyr Tyr	Cys	
85	90	95				
Ala Lys Asp	Ley Thr Asp Ile Val	Ley Met Val	Tyr Val Asp	Tyr Trp		
100	105	110				
Gly Gln Gly	Thr Ley Val	Thr Val Ser	Ser			
115	120					

<210> SEQ ID NO 431
 <211> LENGTH: 322
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence

-continued

<220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 431

```

gacatccaga tgaccaggc tccatcttct gtgtctgc cat ctgttaggaga cagagtcacc      60
atcaacttgctc gggcgagtca ggatattgac aggtggtag cctggatca gcagaaacca      120
gggaaaagccc ctaagtcctt gatctatgct gcatccagg ttgcaaatgg ggtccatca      180
aggttcagcg gcagtggtatc ttcaatctca ctatcagcag cctgcaggct      240
gaagattttg caacttacta ttgtcaacag gctaacagt tgccgttac ttccgggga      300
gggaccaagg tggagatcaa ac                                         322
  
```

<210> SEQ ID NO 432
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 432

```

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1           5           10          15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Asp Arg Trp
20          25          30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35          40          45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50          55          60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65          70          75          80

Glu Asp Phe Ala Thr Tyr Cys Gln Gln Ala Asn Ser Leu Pro Phe
85          90          95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100         105
  
```

<210> SEQ ID NO 433
 <211> LENGTH: 363
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 433

```

cagggtcaat tggtagtgc tggagtttag gtgaagaagc ctggggcctc agtgaaggc      60
tcctgcaaga cttctggta cacttttgc aacaatgggt tcagctgggt gcggcaggcc      120
cctggacaag ggcttgatgg gctggatgg atcagcggtt acaatggaaa cacaaactat      180
gcacagaagt tccaggcag agtcaccatg accacagaca catccacgag tacagctac      240
atggagttga ggactctgag atctgacgac acggccgtct attactgtgc gagagatcg      300
gactacagta acttccactg gctcgacccc tggggccagg gaaccctggt caccgtcgcc      360
tca                                         363
  
```

<210> SEQ ID NO 434
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 434

```

Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala
1           5          10          15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Phe Ser Asn Asn
20          25          30

Gly Phe Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Leu
35          40          45

Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50          55          60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65          70          75          80

Met Glu Leu Arg Thr Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85          90          95

Ala Arg Asp Gln Asp Tyr Ser Asn Phe His Trp Leu Asp Pro Trp Gly
100         105         110

Gln Gly Thr Leu Val Thr Val Ala Ser
115         120

```

<210> SEQ ID NO 435

```

<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 435

ggttacacctt ttagcaacaa tggt

24

```

<210> SEQ ID NO 436
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 436

```

Gly Tyr Thr Phe Ser Asn Asn Gly
1           5

```

```

<210> SEQ ID NO 437
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 437

atcagcggtt acaaatggaaa caca

24

```

<210> SEQ ID NO 438
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 438

```

Ile Ser Gly Tyr Asn Gly Asn Thr
1           5

```

<210> SEQ ID NO 439

259**260**

-continued

<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 439

gcgagagatc aggactacag taacttccac tggctcgacc cc

42

<210> SEQ ID NO 440
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 440

Ala Arg Asp Gln Asp Tyr Ser Asn Phe His Trp Leu Asp Pro
1 5 10

<210> SEQ ID NO 441
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 441

gacatccaga tgacctcagtc tccatccctcc	gtgtctgcat ctgttaggaga cagagtatt	60
atcaattgtc gggcgagtca gggcttttgt agttggcttagt	cctggtatca gcagaaacca	120
gggacacccc ctaagctctt gatccattct	gatccaggat tgcaaactgg ggtcccatca	180
agattcagcg gcagtggtatc tgggacagaa ttcgctctca	ccatcaacag cctgcaggct	240
gaagattttg gaacttacta ttgtcaacag gctaacagtt	tcccgctcac tttcggcggg	300
gggaccagggg tggagatcaa a		321

<210> SEQ ID NO 442
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 442

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Leu Ser Ser Trp
20 25 30Leu Ala Trp Tyr Gln Gln Lys Pro Gly Thr Ala Pro Lys Leu Leu Ile
35 40 45His Ser Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Glu Phe Ala Leu Thr Ile Asn Ser Leu Gln Pro
65 70 75 80Glu Asp Phe Gly Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Leu
85 90 95Thr Phe Gly Gly Gly Thr Arg Val Glu Ile Lys
100 105

<210> SEQ ID NO 443
<211> LENGTH: 18

261

-continued

<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 443

caggggtctta gtagttgg

18

<210> SEQ ID NO 444
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 444

Gln Gly Leu Ser Ser Trp
1 5

<210> SEQ ID NO 445
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 445

tctgcattcc

9

<210> SEQ ID NO 446
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 446

Ser Ala Ser
1

<210> SEQ ID NO 447
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 447

caacaggcta acagttccc gctcact

27

<210> SEQ ID NO 448
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 448

Gln Gln Ala Asn Ser Phe Pro Leu Thr
1 5

<210> SEQ ID NO 449
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

262

-continued

<400> SEQUENCE: 449

```
cagggttcagc tgggtgcagtc tggagtttagt gtgaagaagc ctggggctc agtgaaggc 60
tcctgcaaga cttctggta cacttttagc aacaatggtt tcagctgggt gcggcaggcc 120
cctggacaag ggcttgagtg gctgggatgg atcagcggtt acaaatggaaa cacaaactat 180
gcacagaagt tccagggcag agtcaccatg accacagaca catccacgag tacagctac 240
atggagttga ggactctgag atctgacgac acggccgtct attactgtgc gagagatcg 300
gactacagta acttccactg gctcgacccc tggggccagg gaaccctggt caccgtctcc 360
tca 363
```

<210> SEQ ID NO 450

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 450

```
Gln Val Gln Leu Val Gln Ser Gly Val Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Phe Ser Asn Asn
20 25 30
Gly Phe Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Leu
35 40 45
Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Thr Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Asp Tyr Ser Asn Phe His Trp Leu Asp Pro Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120
```

<210> SEQ ID NO 451

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 451

```
gacatccaga tgaccaggc tccatccctc gtgtctgcat ctgttaggaga cagagtatt 60
atcaacttgtc gggcgagtca gggcttttagt agttggctag cctggatca gcagaaacca 120
gggacagccc ctaagctcct gatccattct gcatccagtt tgcaaactgg ggtccatca 180
agattcagcg gcagtggtatc tgggacagaa ttgcgtctca ccatcaacag cctgcagcct 240
gaagatttt gaaacttacta ttgtcaacag gctaacagtt tcccgctcac tttcgccgg 300
gggaccaagg tggagatcaa a 321
```

<210> SEQ ID NO 452

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

US 9,402,898 B2

265

-continued

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 452

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly			
1	5	10	15

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Leu Ser Ser Trp			
20	25	30	

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Thr Ala Pro Lys Leu Leu Ile			
35	40	45	

His Ser Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly			
50	55	60	

Ser Gly Ser Gly Thr Glu Phe Ala Leu Thr Ile Asn Ser Leu Gln Pro			
65	70	75	80

Glu Asp Phe Gly Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Leu			
85	90	95	

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 453

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 453

cagggttcagc tggtgcaagtc tggagctgag gtgaagaagc ctggggccctc agtgaaggtc	60
--	----

tcctgcagg cttctggta cacttttagc aacaatggta tcagctgggt gcgacaggcc	120
---	-----

cctggacaag ggcttgagtg gatgggatgg atcagcgggt acaaattggaaa cacaaacttat	180
--	-----

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagctac	240
--	-----

atggagctga ggagcctgag atctgacgac acggccgtg attactgtgc gagagatcag	300
--	-----

gactacagta acttccactg gctcgacccc tggggccagg gaaccttgtt caccgtctcc	360
---	-----

tca	363
-----	-----

<210> SEQ ID NO 454

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 454

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala			
1	5	10	15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asn Asn			
20	25	30	

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met			
35	40	45	

Gly Trp Ile Ser Gly Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu			
50	55	60	

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr			
65	70	75	80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys			
85	90	95	

Ala Arg Asp Gln Asp Tyr Ser Asn Phe His Trp Leu Asp Pro Trp Gly			
100	105	110	

266

-continued

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 455
<211> LENGTH: 322
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 455

gacatccaga	tgaccaggc	tccatcttct	gtgtctgc	ctgttaggaga	cagagtccacc	60
atcaacttgtc	gggcgagtca	gggtcttagt	agttggtag	cctggtatca	gcagaaacca	120
ggaaaagccc	ctaagctcct	gatctattct	gcatccagg	tgcaaagtgg	ggtccccatca	180
aggttcagcg	gcagtggtac	tgggacagat	ttcactctca	ctatcagcag	cctgcagcct	240
gaagattttg	caacttacta	ttgtcaacag	gctaacagtt	tcccgtcac	tttcggcgga	300
gggaccaagg	tggagatcaa	ac				322

<210> SEQ ID NO 456
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 456

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val	Ala Ser Val Gly		
1	5	10	15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln	Gly Leu Ser Ser Trp		
20	25	30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro	Lys Leu Leu Ile		
35	40	45	
Tyr Ser Ala Ser Ser Leu Gln Ser Gly Val Pro	Ser Arg Phe Ser Gly		
50	55	60	
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser	Ser Leu Gln Pro		
65	70	75	80
Glu Asp Phe Ala Thr Tyr Cys Gln Gln Ala Asn Ser	Phe Pro Leu		
85	90	95	
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> SEQ ID NO 457
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 457

caggtaagt	tggtgaggc	tggggaggc	gtggtccagc	ctggggaggc	cctgagagtc	60
tccctgtcag	ogtctggatt	caccttcagt	agctatggca	tgcactgggt	ccggccaggct	120
ccaggcaagg	ggctggaggc	gttggcaatt	atatggat	atggagataa	taaatactat	180
tcaagactccg	tgaaggcccg	attcaccatc	tccagagaca	attccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggctgagt	attactgtgt	gagagatgcg	300
agtatagcat	ctcgtttctt	ggactattgg	ggccaggaa	ccttggtcac	cgtctccat	360

-continued

```

<210> SEQ ID NO 458
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 458

Gln Val Lys Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1           5          10          15

Ser Leu Arg Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20          25          30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35          40          45

Ala Ile Ile Trp Tyr Asp Gly Asp Asn Lys Tyr Tyr Ser Asp Ser Val
50          55          60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65          70          75          80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Glu Tyr Tyr Cys
85          90          95

Val Arg Asp Ala Ser Ile Ala Ser Arg Phe Leu Asp Tyr Trp Gly Gln
100         105         110

Gly Thr Leu Val Thr Val Ser Ser
115         120

```

```

<210> SEQ ID NO 459
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 459

ggattcacct tcagtagcta tggc

24

```

<210> SEQ ID NO 460
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 460

Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

```

<210> SEQ ID NO 461
<211> LENGTH: 24
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

<400> SEQUENCE: 461

atatggatg atggagataa taaa

24

```

<210> SEQ ID NO 462
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

```

-continued

<400> SEQUENCE: 462

Ile Trp Tyr Asp Gly Asp Asn Lys
1 5<210> SEQ ID NO 463
<211> LENGTH: 39
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 463

gtgagagatg cgagtagatgc atctcgtttc ttggactat 39

<210> SEQ ID NO 464
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 464

Val Arg Asp Ala Ser Ile Ala Ser Arg Phe Leu Asp Tyr
1 5 10<210> SEQ ID NO 465
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 465

gacatccaga tgacctcagtc tccatcctca ctgtctgcat ctataggaga cagagtacc 60
atcacttgc gggcgactca ggacattaac aattattnag cctggttca gcagaaacca 120
gggaaaagccc ctaagtccct gatctatgct acatccaatt tgcaaagtgg ggtcccatca 180
aagttcagcg gcagtggtac tgggacagat tacactctca ccatcagcag cctgcagcct 240
gaagatttt caacttatta ctgtcaacag tatcatagtt acccgctcac tttcgccgga 300
gggaccaagg tggagatcaa a 321<210> SEQ ID NO 466
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 466

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Ile Gly
1 5 10 15Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Gln Asp Ile Asn Asn Tyr
20 25 30Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35 40 45Tyr Ala Thr Ser Asn Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
50 55 60Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80Glu Asp Phe Ser Thr Tyr Tyr Cys Gln Gln Tyr His Ser Tyr Pro Leu
85 90 95

-continued

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 467
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 467

caggacattt acaattat

18

<210> SEQ ID NO 468
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 468

Gln Asp Ile Asn Asn Tyr
1 5

<210> SEQ ID NO 469
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 469

gctacatcc

9

<210> SEQ ID NO 470
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 470

Ala Thr Ser
1

<210> SEQ ID NO 471
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 471

caacagtatc atagttaccc gctcact

27

<210> SEQ ID NO 472
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 472

Gln Gln Tyr His Ser Tyr Pro Leu Thr
1 5

-continued

<210> SEQ ID NO 473
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 473

```
caggtgcagc tgggggaggc gtgggtccagc ctggggaggc cctgagatc      60
tcctgtgcag cgtctggatt caccttcaat agctatggca tgcactgggt ccgccaggct    120
ccaggcaagg ggctggaggc gttggcaatt atatggatg atggagataa taaataactat    180
tcagactccg tgaagggccg attaccatc tccagagaca attccaagaa cacgctgtat    240
ctgcaaataatgac acagcctgag agccgaggac acggctgagttt attactgtgt gagagatgcg    300
agtatacgat ctcgtttctt ggactattgg ggccaggaa ccctggtcac cgtctccctca    360
```

<210> SEQ ID NO 474
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 474

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1															
Ser	Leu	Arg	Val	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr
20															
Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu
35															
Ala	Ile	Ile	Trp	Tyr	Asp	Gly	Asp	Asn	Lys	Tyr	Tyr	Ser	Asp	Ser	Val
50															
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65															
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Glu	Tyr	Tyr	Cys
85															
Val	Arg	Asp	Ala	Ser	Ile	Ala	Ser	Arg	Phe	Leu	Asp	Tyr	Trp	Gly	Gln
100															
Gly	Thr	Leu	Val	Thr	Val	Ser	Ser								
115															

<210> SEQ ID NO 475
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 475

```
gacatccaga tgaccaggc tccatccatca ctgtctgcat ctataggaga cagagtccacc      60
atcacttgcc gggcgcactca ggacattaac aattatgg cctgggttca gcagaaacca    120
gggaaaagcccc ctaagtcctt gatctatgct acatccaatt tgcaaagtgg ggtcccatca    180
aagttcagcg gcagtggttc tgggacat tacactctca ccatcagcag cctgcagcct    240
gaagatttt caacttattt ctgtcaacag tatcatatgtt acccgctcac tttcggcgaa    300
gggaccaagg tggagatcaa a                                         321
```

-continued

<210> SEQ ID NO 476
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 476

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Ile	Gly
1							5			10					15

Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Gln Asp Ile Asn Asn Tyr
20 25 30

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
35 40 45

Tyr Ala Thr Ser Asn Leu Gln Ser Gly Val Pro Ser Lys Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ser Thr Tyr Tyr Cys Gln Gln Tyr His Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> SEQ ID NO 477
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 477

caggtgcagc	tggtgagtc	tggggaggc	gtggtccagc	ctgggaggc	cctgagactc	60
tccctgtgcag	cgtctggatt	cacttcagt	agctatggca	tgcactgggt	ccgccaggct	120
ccaggcaagg	ggctggagtg	ggtggcagtt	atatggat	atggagataa	taaatactat	180
gcagactccg	tgaaggcccg	attcaccatc	tccagagaca	actccaagaa	cacgctgtat	240
ctgcaaatga	acagcctgag	agccgaggac	acggctgtgt	attactgtgt	gagagatgcg	300
agtatagcat	ctcgtttctt	ggactattgg	ggccaggaa	ccctggtcac	cgtctccctca	360

<210> SEQ ID NO 478
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 478

Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
1							5		10					15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Trp Tyr Asp Gly Asp Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

-continued

Val Arg Asp Ala Ser Ile Ala Ser Arg Phe Leu Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 479

<211> LENGTH: 322

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 479

gacatccaga tgaccaggc	tccatcctca ctgtctgcat	ctgttaggaga cagagtacc	60
atcaacttgtc gggcgagtca ggacattaac aattattn	tag cctggttca gcagaaacca	120	
gggaaagccc otaagtcct gatctatgct acatccagtt	tgcaaagtgg ggtcccatca	180	
aggttcagcg gcagtggtatc tgggacatgtt tcactctca	ccatcagcag cctgcagcct	240	
gaagattttg caacttatta ctgccaacag tatcatagtt	acccgctcac tttcggcgga	300	
gggaccaagg tggagatcaa ac		322	

<210> SEQ ID NO 480

<211> LENGTH: 107

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 480

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly		
1 5 10 15		

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr		
20 25 30		

Leu Ala Trp Phe Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile		
35 40 45		

Tyr Ala Thr Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly		
50 55 60		

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro		
65 70 75 80		

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr His Ser Tyr Pro Leu		
85 90 95		

Thr Phe Gly Gly Thr Lys Val Glu Ile Lys		
100 105		

<210> SEQ ID NO 481

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 481

gaggtgcaac tggggaggc tggggaggac ttggtagc	ctggggggtc cctgagactc	60
tccctgtgcag cctctgaatt cacctttagc ggctatgcca	tgagctgggt ccggcaggct	120
ccagggagg ggctggaggc ggtctcgttg attcgtggta	gtggtgataa cacatactac	180
gcagactccg tgaaggggccg gttcagcatac tccagagaca	attccaagaa cacactgtat	240
ctgcaaatacg acagcctgag agccgaggac acggccgtat	attactgtgc gagagtgtat	300

-continued

tacgattttt gggaaaggggc ttttgatatac tggggccaaag ggacaatggt caccgtctct 360
 tca 363

<210> SEQ ID NO 482
 <211> LENGTH: 121
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic
 <400> SEQUENCE: 482
 Glu Val Gln Leu Leu Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Glu Phe Thr Phe Ser Gly Tyr
 20 25 30
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Val Ile Arg Gly Ser Gly Asp Asn Thr Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Ser Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Val Tyr Tyr Asp Phe Trp Glu Gly Ala Phe Asp Ile Trp Gly
 100 105 110
 Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 483
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic
 <400> SEQUENCE: 483
 gaattcacct ttageggcta tgcc 24

<210> SEQ ID NO 484
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic
 <400> SEQUENCE: 484
 Glu Phe Thr Phe Ser Gly Tyr Ala
 1 5

<210> SEQ ID NO 485
 <211> LENGTH: 24
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic
 <400> SEQUENCE: 485
 attcgtggta gtgggtataa caca 24

<210> SEQ ID NO 486
 <211> LENGTH: 8

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 486

Ile Arg Gly Ser Gly Asp Asn Thr
1 5

<210> SEQ ID NO 487
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 487

gcgagagtgt attacgattt ttggaaaggg gctttgata tc 42

<210> SEQ ID NO 488
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 488

Ala Arg Val Tyr Tyr Asp Phe Trp Glu Gly Ala Phe Asp Ile
1 5 10

<210> SEQ ID NO 489
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 489

gacatccaga tgaccaggc tccatcttcc gtgtctgcat ctgttaggaga cagagtacc 60
atcaacttgtc gggcgagtca gggttattgc acctggtag cctggtatca gcagaaacca 120
gggaaaagccc ctaagctcct gatctatgc gcaaccaggc tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggtac tgggacagat ttcactctcg ccatcagccg cctgcaggct 240
gaagattttg caacttacta ttgtcaacag gctaacaatt tcccgtagac ttttggccag 300
gggaccaagc tggagatcaa a 321

<210> SEQ ID NO 490
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 490

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Thr Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

-continued

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Gly Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Asn Phe Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> SEQ ID NO 491
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 491

cagggttatta gcacctgg

18

<210> SEQ ID NO 492
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 492

Gln Gly Ile Ser Thr Trp
1 5

<210> SEQ ID NO 493
<211> LENGTH: 9
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 493

gctgcaacc

9

<210> SEQ ID NO 494
<211> LENGTH: 3
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 494

Ala Ala Thr
1

<210> SEQ ID NO 495
<211> LENGTH: 27
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 495

caacaggcta acaatttccc gtacact

27

<210> SEQ ID NO 496
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

-continued

<400> SEQUENCE: 496

Gln Gln Ala Asn Asn Phe Pro Tyr Thr
1 5

<210> SEQ ID NO 497

<211> LENGTH: 363

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 497

gaggtgcagc	tgtggagtc	tgggggagac	tgggtacagc	ctggggggtc	cctgagactc	60
tccctgtgcag	cctctgaatt	cacctttagc	ggctatgeca	tgagctgggt	ccgcccaggct	120
ccagggaaagg	ggctggagtg	ggtctcagtg	attcgtggta	gtggtgataa	cacataactac	180
gcagactccg	tgaagggccg	gttcagcatc	tccagagaca	attccaagaa	cacactgtat	240
ctgcaaatga	acagectgag	agccgaggac	acggccgtat	attactgtgc	gagagtgtat	300
tacgattttt	ggaaaggggc	ttttgatatc	tggggccaag	ggacaatggt	caccgtctct	360
tca						363

<210> SEQ ID NO 498

<211> LENGTH: 121

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 498

Glu	Val	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Asp	Leu	Val	Gln	Pro	Gly	Gly
1					5				10			15			

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Glu	Phe	Thr	Phe	Ser	Gly	Tyr
					20				25			30			

Ala	Met	Ser	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
					35			40			45				

Ser	Val	Ile	Arg	Gly	Ser	Gly	Asp	Asn	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
					50			55			60				

Lys	Gly	Arg	Phe	Ser	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr
65					70			75			80				

Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
					85			90			95				

Ala	Arg	Val	Tyr	Tyr	Asp	Phe	Trp	Glu	Gly	Ala	Phe	Asp	Ile	Trp	Gly
					100			105			110				

Gln	Gly	Thr	Met	Val	Thr	Val	Ser	Ser							
					115			120							

<210> SEQ ID NO 499

<211> LENGTH: 321

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 499

gacatccaga	tgacccagtc	tccatcttcc	gtgtctgcat	ctgttaggaga	cagagtccacc	60
atcacttgtc	gggcgagtca	gggtttagc	acctggtag	cctggtatca	gcagaaacca	120
gggaaagccc	ctaagctcct	gatctatgct	gcaaccagg	tgcaaagtgg	ggtccccatca	180

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289**290**

-continued

aggttcagcg gcagtggatc tgggacagat ttcaactctcg ccatcagccg cctgcagccct	240
gaagatttt caacttacta ttgtcaacag gctaacaatt tcccgtacac ttttggccag	300
gggaccaagc tggagatcaa a	321

<210> SEQ ID NO 500
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 500

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly			
1	5	10	15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Thr Trp			
20	25	30	
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile			
35	40	45	
Tyr Ala Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly			
50	55	60	
Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Gly Leu Gln Pro			
65	70	75	80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Asn Phe Pro Tyr			
85	90	95	
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys			
100	105		

<210> SEQ ID NO 501
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 501

gaggtgcagc tgttggagtc tgggggaggc ttggtagc ctggggggc cctgagactc	60
tcctgtgcag cctctgaatt cacctttagc ggctatgcc a tgagctgggt ccgccaggct	120
ccagggaaagg ggctggagtg ggtctcagct attcgtggta gtggataa cacataactac	180
gcagactccg tgaaggccg gttcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaaattga acagcctgag agccgaggac acggccgtat attactgtgc gagagtgtat	300
tacgattttt gggaaaggggc ttttgatatc tggggccaag ggacaatggt caccgtctct	360
tca	363

<210> SEQ ID NO 502
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 502

Glu Val Gln Leu Leu Glu Ser Gly Gly Leu Val Gln Pro Gly Gly			
1	5	10	15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Glu Phe Thr Phe Ser Gly Tyr			
20	25	30	
Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
35	40	45	

-continued

Ser Ala Ile Arg Gly Ser Gly Asp Asn Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Val Tyr Tyr Asp Phe Trp Glu Gly Ala Phe Asp Ile Trp Gly
 100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> SEQ ID NO 503
 <211> LENGTH: 322
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 503

gacatccaga tgaccaggc tccatcttct gtgtctgcat ctgttaggaga cagagtccacc 60
 atcaacttgtc gggcgagtca gggatttagc acctggtag cctggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcaaccagg tgc当地 agtgg ggtcccatca 180
 aggttcagcg gcagtggtac tggacagat ttcaacttca ctatcagcag cctgcagcct 240
 gaagattttg caacttacta ttgtcaacag gctaacaatt tccctgtacac ttttggccag 300
 gggaccaagc tggagatcaa ac 322

<210> SEQ ID NO 504
 <211> LENGTH: 107
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 504

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Thr Trp
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ala Ala Thr Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Cys Gln Gln Ala Asn Asn Phe Pro Tyr
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> SEQ ID NO 505
 <211> LENGTH: 357
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 505

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caggtgcagc tggtgaggc tgggggaggc gtggtccagc ctgggaggc cctgagactc	60
tccctgtcgac cgtctggatt caccttcagt gcctatggca tgcactgggt ccgccaggct	120
ccaggcaagg ggctggaggc ggtggcaatt atatggtagt atggaaagtaa taaatactac	180
gcagactccg tgaaggccg attcaccatc tccagagaca attccaagaa cacgctgtat	240
ctgcaaattga acagcctgag agccgaggac acggctgtgt attattgtgc gagagaggat	300
acctcttatgg ttctctttga ctactggggc cagggAACCC tggtcacccgt ctccctca	357

<210> SEQ ID NO 506

<211> LENGTH: 119

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 506

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg	
1 5 10 15	

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ala Tyr	
20 25 30	

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val	
35 40 45	

Ala Ile Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val	
50 55 60	

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr	
65 70 75 80	

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	

Ala Arg Glu Asp Thr Ser Met Val Leu Phe Asp Tyr Trp Gly Gln Gly	
100 105 110	

Thr Leu Val Thr Val Ser Ser	
115	

<210> SEQ ID NO 507

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 507

ggattcacct tcagtccta tggc	24
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<210> SEQ ID NO 508

<211> LENGTH: 8

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 508

Gly Phe Thr Phe Ser Ala Tyr Gly	
1 5	

<210> SEQ ID NO 509

<211> LENGTH: 24

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

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<400> SEQUENCE: 509

```
atatggtagt atggaagtaa taaa
<210> SEQ ID NO 510
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 510

Ile Trp Tyr Asp Gly Ser Asn Lys	
1	5

```
<210> SEQ ID NO 511
<211> LENGTH: 36
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 511

gcgagagagg atacctctat ggttctcttt gactac

36

```
<210> SEQ ID NO 512
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 512

Ala Arg Glu Asp Thr Ser Met Val Leu Phe Asp Tyr		
1	5	10

```
<210> SEQ ID NO 513
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 513

```
caggtgcagc tggtgagtc tgggggaggc gtggtccagc ctgggaggc cctgagactc 60
tcctgtgcag cgtctggatt caccttcagt gcctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcaatt atatggtagt atggaagtaa taaatactac 180
geagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagectgag agccgaggac acggctgtgt attattgtgc gagagaggat 300
acctctatgg ttctcttga ctactggggc cagggAACCC tggcacccgt ctccctca 357
```

```
<210> SEQ ID NO 514
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic
```

<400> SEQUENCE: 514

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg			
1	5	10	15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ala Tyr		
20	25	30

-continued

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Ile Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Glu Asp Thr Ser Met Val Leu Phe Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 515

<211> LENGTH: 357

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 515

caggtgcagc tggtgagtc tgggggaggc gtggtccagc ctgggaggc cctgagactc 60
 tcctgtcgac cgtctggatt caccttcagt gcctatggca tgcactgggt ccgccaggct 120
 ccaggcaagg ggcttagagtg ggtggcagtt atatggatg atggaagtaa taaatactat 180
 gcagactccg tgaaggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatga acagectgag agccgaggac acggctgtgt attactgtgc gagagaggat 300
 acctctatgg ttctcttga ctactggggc cagggAACCC tggtcaccgt ctccctca 357

<210> SEQ ID NO 516

<211> LENGTH: 119

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 516

Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ala Tyr
 20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Glu Asp Thr Ser Met Val Leu Phe Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ser
 115

<210> SEQ ID NO 517

<211> LENGTH: 1488

<212> TYPE: DNA

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<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 517

atgtggcaga ttgtttctt tactctgagc tgcgtatcttgc tcttggccgc agcctataac	60
aactttcggaa agagcatggaa cagcataggaa aagaagcaat atcaggatcca gcatgggtcc	120
tgcagctaca ctttcttcctt gccagagatg gacaactgcg gctttccctc cagccccctac	180
gtgtccaatgt ctgtgcagag ggacgcgcgc ctcgaataacg atgactcggt gcagaggctg	240
caagtgcgtgg agaacatcat ggaaaacaac actcagtggc taatgaagct tgagaatttat	300
atccaggaca acatgaagaa agaaatggta gagatacagc agaatgcagt acagaaccag	360
acggcgtgtga tggatagaaat agggacaaac ctgttgaacc aaacagctga gcaaaccgcgg	420
aagtttaactg atgttggaaagc ccaagtatttta aatcagacca cgagacttga acttcagctc	480
ttggAACACT ccctctcgac aaacaaatttgg gaaaaacaga ttttggacca gaccagtgaa	540
ataaaacaaat tgcaagataa gaacagtttc ctagaaaaga aggtgcgtac tatggaaagac	600
aagcacatca tccaaactaca gtcaataaaaaa gaagagaaaag atcagctaca ggtgttagta	660
tccaaagcaaa attccatcat tgaagaacta gaaaaaaaaa tagtgcgtac cacggtaat	720
aattcagttc ttccaaagca gcaacatgtat ctcatggaga cagttataaa cttactgact	780
atgatgtcca catcaaactc agctaaggac cccactgttg ctaaagaaga acaaattcagc	840
ttcagagact gtgcgtggat attcaaatca ggacacacca caaatggcat ctacacgtta	900
acattcccta attctacaga agagatcaag gcctactgtg acatggaaac tggaggaggc	960
gggtggacaa ttattcagcg acgtgaggat ggcagcgttg atttcagag gacttggaaa	1020
gaatataaaag tgggattttgg taacccttca ggagaatattt ggctggggaaa tgagttgtt	1080
tcgcaactga ctaatcagca acgctatgtg cttaaaatac accttaaaga ctggaaagg	1140
aatgaggctt actcattgtt tgaacatttc tatctctcaa gtgaagaact caattatagg	1200
attcacctta aaggacttac agggacagcc ggcaaaataa gcagcatcag ccaaccagga	1260
aatgatttttta gcacaaagga tggagacaac gacaaatgtt tttgcaaatg ttcacaaatg	1320
ctaacaggag gctgggtggtt tggatgcattt ggtccttca acgttgcgtt aatgtactat	1380
ccacagaggc agaacacaaa taagttcaac ggcattaaat ggtactactg gaaaggctca	1440
ggctattcgc tcaaggccac aaccatgttgc atccgaccag cagatttc	1488

<210> SEQ ID NO 518

<211> LENGTH: 496

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 518

Met Trp Gln Ile Val Phe Phe Thr Leu Ser Cys Asp Leu Val Leu Ala			
1	5	10	15

Ala Ala Tyr Asn Asn Phe Arg Lys Ser Met Asp Ser Ile Gly Lys Lys		
20	25	30

Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro		
35	40	45

Glu Met Asp Asn Cys Arg Ser Ser Ser Pro Tyr Val Ser Asn Ala		
50	55	60

Val Gln Arg Asp Ala Pro Leu Glu Tyr Asp Asp Ser Val Gln Arg Leu

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65	70	75	80
Gln Val Leu Glu Asn Ile Met Glu Asn Asn Thr Gln Trp			
85	90	95	
Leu Glu Asn Tyr Ile Gln Asp Asn Met Lys Lys Glu Met	Val	Glu Ile	
100	105	110	
Gln Gln Asn Ala Val Gln Asn Gln Thr Ala Val Met Ile	Glu Ile Gly		
115	120	125	
Thr Asn Leu Leu Asn Gln Thr Ala Glu Gln Thr Arg Lys	Leu Thr Asp		
130	135	140	
Val Glu Ala Gln Val Leu Asn Gln Thr Thr Arg	Leu Glu Leu Gln Leu		
145	150	155	160
Leu Glu His Ser Leu Ser Thr Asn Lys Leu Glu Lys Gln Ile	Leu Asp		
165	170	175	
Gln Thr Ser Glu Ile Asn Lys Leu Gln Asp Lys Asn Ser Phe	Leu Glu		
180	185	190	
Lys Lys Val Leu Ala Met Glu Asp Lys His Ile Ile Gln	Leu Gln Ser		
195	200	205	
Ile Lys Glu Glu Lys Asp Gln Leu Gln Val Leu Val Ser Lys	Gln Asn		
210	215	220	
Ser Ile Ile Glu Glu Leu Glu Lys Ile Val Thr Ala Thr Val	Asn		
225	230	235	240
Asn Ser Val Leu Gln Lys Gln His Asp Leu Met Glu Thr Val	Asn		
245	250	255	
Asn Leu Leu Thr Met Met Ser Thr Ser Asn Ser Ala Lys Asp	Pro Thr		
260	265	270	
Val Ala Lys Glu Glu Gln Ile Ser Phe Arg Asp Cys Ala	Glu Val Phe		
275	280	285	
Lys Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr	Phe Pro Asn		
290	295	300	
Ser Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala	Gly Gly		
305	310	315	320
Gly Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val	Asp Phe Gln		
325	330	335	
Arg Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro	Ser Gly Glu		
340	345	350	
Tyr Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn	Gln Gln Arg		
355	360	365	
Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn	Glu Ala Tyr		
370	375	380	
Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu	Asn Tyr Arg		
385	390	395	400
Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile	Ser Ser Ile		
405	410	415	
Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp	Asn Asp Lys		
420	425	430	
Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly	Gly Trp Trp Phe Asp		
435	440	445	
Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr	Pro Gln Arg Gln		
450	455	460	
Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr	Trp Lys Gly Ser		
465	470	475	480
Gly Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro	Ala Asp Phe		
485	490	495	

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<210> SEQ_ID NO 519
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 519

Arg	Asp	Cys	Ala	Glu	Val	Phe	Lys	Ser	Gly	His	Thr	Thr	Asn	Gly	Ile
1			5			10							15		

Tyr

Tyr	Thr	Leu	Thr	Phe	Pro	Asn	Ser	Thr	Glu	Glu	Ile	Lys	Ala	Tyr	Cys
20				25								30			

Asp

Asp	Met	Glu	Ala	Gly	Gly	Gly	Trp	Thr	Ile	Ile	Gln	Arg	Arg	Glu
35				40								45		

Asp

Asp	Gly	Ser	Val	Asp	Phe	Gln	Arg	Thr	Trp	Lys	Glu	Tyr	Lys	Val	Gly
50				55						60					

Phe

Phe	Gly	Asn	Pro	Ser	Gly	Glu	Tyr	Trp	Leu	Gly	Asn	Glu	Phe	Val	Ser
65					70				75			80			

Gln

Gln	Leu	Thr	Asn	Gln	Gln	Arg	Tyr	Val	Leu	Lys	Ile	His	Leu	Lys	Asp
85					90						95				

Trp

Trp	Glu	Gly	Asn	Glu	Ala	Tyr	Ser	Leu	Tyr	Glu	His	Phe	Tyr	Leu	Ser
100					105				110						

Ser

Ser	Glu	Glu	Leu	Asn	Tyr	Arg	Ile	His	Leu	Lys	Gly	Leu	Thr	Gly	Thr
115					120				125						

Ala

Ala	Gly	Lys	Ile	Ser	Ser	Ile	Ser	Gln	Pro	Gly	Asn	Asp	Phe	Ser	Thr
130					135				140						

Lys

Lys	Asp	Gly	Asp	Asn	Asp	Lys	Cys	Ile	Cys	Lys	Cys	Ser	Gln	Met	Leu
145					150				155			160			

Thr

Thr	Gly	Gly	Trp	Trp	Phe	Asp	Ala	Cys	Gly	Pro	Ser	Asn	Leu	Asn	Gly
165					170				175						

Met

Met	Tyr	Tyr	Pro	Gln	Arg	Gln	Asn	Thr	Asn	Lys	Phe	Asn	Gly	Ile	Lys
180					185					190					

Trp

Trp	Tyr	Tyr	Trp	Lys	Gly	Ser	Gly	Tyr	Ser	Leu	Lys	Ala	Thr	Thr	Met
195					200					205					

Met

Met	Ile	Arg	Pro	Ala	Asp	Phe
210					215	

<210> SEQ_ID NO 520
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 520

Arg	Asp	Cys	Ala	Glu	Ile	Phe	Lys	Ser	Gly	Leu	Thr	Thr	Ser	Gly	Ile
1			5			10							15		

Tyr

Tyr	Thr	Leu	Thr	Phe	Pro	Asn	Ser	Thr	Glu	Glu	Ile	Lys	Ala	Tyr	Cys
20				25								30			

Asp

Asp	Met	Asp	Val	Gly	Gly	Gly	Trp	Thr	Val	Ile	Gln	His	Arg	Glu	
35				40								45			

Asp

Asp	Gly	Ser	Val	Asp	Phe	Gln	Arg	Thr	Trp	Lys	Glu	Tyr	Lys	Glu	Gly
50					55				60						

Phe

Phe	Gly	Ser	Pro	Leu	Gly	Glu	Tyr	Trp	Leu	Gly	Asn	Glu	Phe	Val	Ser
65				70					75			80			

Gln

Gln	Leu	Thr	Gly	Gln	His	Arg	Tyr	Val	Leu	Lys	Ile	Gln	Leu	Lys	Asp
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

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85	90	95
Trp Glu Gly Asn Glu Ala His Ser Leu Tyr Asp His Phe Tyr Leu Ala		
100	105	110
Gly Glu Glu Ser Asn Tyr Arg Ile His Leu Thr Gly Leu Thr Gly Thr		
115	120	125
Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Ser Asp Phe Ser Thr		
130	135	140
Lys Asp Ser Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu		
145	150	155
Ser Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly		
165	170	175
Gln Tyr Tyr Pro Gln Lys Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys		
180	185	190
Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met		
195	200	205
Met Ile Arg Pro Ala Asp Phe		
210	215	

<210> SEQ_ID NO 521
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 521

Arg Asp Cys Ala Glu Val Phe Lys Ser Gly His Thr Thr Asn Gly Val		
1	5	10
Tyr Thr Leu Thr Leu Pro Asn Ser Thr Glu Glu Val Lys Ala Tyr Cys		
20	25	30
Asp Met Glu Ala Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu		
35	40	45
Asp Gly Ser Val Asp Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly		
50	55	60
Phe Gly Asn Pro Ser Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser		
65	70	75
Gln Leu Thr Asn Gln Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp		
85	90	95
Trp Glu Gly Asn Glu Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser		
100	105	110
Ser Glu Glu Leu Asn Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr		
115	120	125
Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr		
130	135	140
Lys Asp Ala Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu		
145	150	155
Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly		
165	170	175
Met Tyr Tyr Pro Gln Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys		
180	185	190
Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Gly Thr Thr Met		
195	200	205
Met Ile Arg Pro Ala Asp Phe		
210	215	

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<210> SEQ_ID NO 522
<211> LENGTH: 674
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 522

Arg Asp Cys Ala Glu Val Phe Lys Ser Gly His Thr Thr Asn Gly Ile
1           5          10          15

Tyr Thr Leu Thr Phe Pro Asn Ser Thr Glu Glu Ile Lys Ala Tyr Cys
20          25          30

Asp Met Glu Ala Gly Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu
35          40          45

Asp Gly Ser Val Asp Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly
50          55          60

Phe Gly Asn Pro Ser Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser
65          70          75          80

Gln Leu Thr Asn Gln Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp
85          90          95

Trp Glu Gly Asn Glu Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser
100         105         110

Ser Glu Glu Leu Asn Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr
115         120         125

Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr
130         135         140

Lys Asp Gly Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu
145         150         155         160

Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly
165         170         175

Met Tyr Tyr Pro Gln Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys
180         185         190

Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met
195         200         205

Met Ile Arg Pro Ala Asp Phe Gly Gly Pro Gly Glu Pro Lys Ser Cys
210         215         220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225         230         235         240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245         250         255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260         265         270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275         280         285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290         295         300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305         310         315         320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325         330         335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340         345         350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
355         360         365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu

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370	375	380
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro		
385	390	395
400		
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val		
405	410	415
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met		
420	425	430
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser		
435	440	445
Pro Gly Lys Gly Gly Gly Ser Gly Ala Pro Arg Asp Cys Ala Glu		
450	455	460
Val Phe Lys Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr Phe		
465	470	475
480		
Pro Asn Ser Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala Gly		
485	490	495
Gly Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val Asp		
500	505	510
Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro Ser		
515	520	525
Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn Gln		
530	535	540
Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu		
545	550	555
560		
Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn		
565	570	575
Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser		
580	585	590
Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn		
595	600	605
Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp		
610	615	620
Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln		
625	630	635
640		
Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr Trp Lys		
645	650	655
Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro Ala		
660	665	670
Asp Phe		
<210> SEQ ID NO 523		
<211> LENGTH: 663		
<212> TYPE: PRT		
<213> ORGANISM: Artificial Sequence		
<220> FEATURE:		
<223> OTHER INFORMATION: synthetic		
<400> SEQUENCE: 523		
Arg Asp Cys Ala Glu Val Phe Lys Ser Gly His Thr Thr Asn Gly Ile		
1	5	10
		15
Tyr Thr Leu Thr Phe Pro Asn Ser Thr Glu Glu Ile Lys Ala Tyr Cys		
20	25	30
Asp Met Glu Ala Gly Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu		
35	40	45
Asp Gly Ser Val Asp Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly		
50	55	60

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Phe Gly Asn Pro Ser Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser
65 70 75 80

Gln Leu Thr Asn Gln Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp
85 90 95

Trp Glu Gly Asn Glu Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser
100 105 110

Ser Glu Glu Leu Asn Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr
115 120 125

Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr
130 135 140

Lys Asp Gly Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu
145 150 155 160

Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly
165 170 175

Met Tyr Tyr Pro Gln Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys
180 185 190

Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met
195 200 205

Met Ile Arg Pro Ala Asp Phe Glu Pro Arg Gly Pro Thr Ile Lys Pro
210 215 220

Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Pro Ser
225 230 235 240

Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu
245 250 255

Ser Pro Ile Val Thr Cys Val Val Asp Val Ser Glu Asp Asp Pro
260 265 270

Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala
275 280 285

Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val
290 295 300

Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe
305 310 315 320

Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr
325 330 335

Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu
340 345 350

Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys
355 360 365

Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn
370 375 380

Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys
405 410 415

Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
420 425 430

Leu His Asn His His Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
435 440 445

Arg Asp Cys Ala Glu Val Phe Lys Ser Gly His Thr Thr Asn Gly Ile
450 455 460

Tyr Thr Leu Thr Phe Pro Asn Ser Thr Glu Glu Ile Lys Ala Tyr Cys
465 470 475 480

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Asp Met Glu Ala Gly Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu
 485 490 495
 Asp Gly Ser Val Asp Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly
 500 505 510
 Phe Gly Asn Pro Ser Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser
 515 520 525
 Gln Leu Thr Asn Gln Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp
 530 535 540
 Trp Glu Gly Asn Glu Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser
 545 550 555 560
 Ser Glu Glu Leu Asn Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr
 565 570 575
 Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr
 580 585 590
 Lys Asp Gly Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu
 595 600 605
 Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly
 610 615 620
 Met Tyr Tyr Pro Gln Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys
 625 630 635 640
 Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met
 645 650 655
 Met Ile Arg Pro Ala Asp Phe
 660

<210> SEQ_ID NO 524
 <211> LENGTH: 448
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: synthetic

 <400> SEQUENCE: 524

 Arg Asp Cys Ala Glu Val Phe Lys Ser Gly His Thr Thr Asn Gly Ile
 1 5 10 15
 Tyr Thr Leu Thr Phe Pro Asn Ser Thr Glu Glu Ile Lys Ala Tyr Cys
 20 25 30
 Asp Met Glu Ala Gly Gly Gly Trp Thr Ile Ile Gln Arg Arg Glu
 35 40 45
 Asp Gly Ser Val Asp Phe Gln Arg Thr Trp Lys Glu Tyr Lys Val Gly
 50 55 60
 Phe Gly Asn Pro Ser Gly Glu Tyr Trp Leu Gly Asn Glu Phe Val Ser
 65 70 75 80
 Gln Leu Thr Asn Gln Gln Arg Tyr Val Leu Lys Ile His Leu Lys Asp
 85 90 95
 Trp Glu Gly Asn Glu Ala Tyr Ser Leu Tyr Glu His Phe Tyr Leu Ser
 100 105 110
 Ser Glu Glu Leu Asn Tyr Arg Ile His Leu Lys Gly Leu Thr Gly Thr
 115 120 125
 Ala Gly Lys Ile Ser Ser Ile Ser Gln Pro Gly Asn Asp Phe Ser Thr
 130 135 140
 Lys Asp Gly Asp Asn Asp Lys Cys Ile Cys Lys Cys Ser Gln Met Leu
 145 150 155 160
 Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly
 165 170 175

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Met Tyr Tyr Pro Gln Arg Gln Asn Thr Asn Lys Phe Asn Gly Ile Lys
 180 185 190
 Trp Tyr Tyr Trp Lys Gly Ser Gly Tyr Ser Leu Lys Ala Thr Thr Met
 195 200 205
 Met Ile Arg Pro Ala Asp Phe Glu Pro Arg Gly Pro Thr Ile Lys Pro
 210 215 220
 Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro Ser
 225 230 235 240
 Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu
 245 250 255
 Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro
 260 265 270
 Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala
 275 280 285
 Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg Val Val
 290 295 300
 Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys Glu Phe
 305 310 315 320
 Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr
 325 330 335
 Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr Val Leu
 340 345 350
 Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu Thr Cys
 355 360 365
 Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn
 370 375 380
 Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp
 385 390 395 400
 Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu Lys Lys
 405 410 415
 Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
 420 425 430
 Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
 435 440 445

<210> SEQ ID NO 525

<211> LENGTH: 981

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 525

Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1 5 10 15
 Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
 20 25 30
 Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
 35 40 45
 Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
 50 55 60
 Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
 65 70 75 80
 Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
 85 90 95

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Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
 100 105 110
 Ile Arg Thr Met Lys Met Arg Gln Gln Ala Ser Phe Leu Pro Ala Thr
 115 120 125
 Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
 130 135 140
 Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
 145 150 155 160
 Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
 165 170 175
 His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
 180 185 190
 Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
 195 200 205
 Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
 210 215 220
 Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
 225 230 235 240
 Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
 245 250 255
 Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
 260 265 270
 Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
 275 280 285
 Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
 290 295 300
 Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
 305 310 315 320
 Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
 325 330 335
 Gly Leu Gln Cys Glu Arg Glu Gly Ile Pro Arg Met Thr Pro Lys Ile
 340 345 350
 Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
 355 360 365
 Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
 370 375 380
 Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
 385 390 395 400
 Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
 405 410 415
 Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
 420 425 430
 Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
 435 440 445
 Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
 450 455 460
 Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
 465 470 475 480
 Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
 485 490 495
 Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
 500 505 510
 Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Glu Gly

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515	520	525
His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro		
530	535	540
Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn		
545	550	555
Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val		
565	570	575
Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys		
580	585	590
Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg		
595	600	605
Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu		
610	615	620
Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro		
625	630	635
Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val		
645	650	655
Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile		
660	665	670
Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys		
675	680	685
Ile Lys Asn Ala Thr Ile Ile Gln Tyr Gln Leu Lys Gly Leu Glu Pro		
690	695	700
Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser		
705	710	715
Ser Asn Pro Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln		
725	730	735
Ala Pro Ala Asp Leu Gly Gly Lys Gly Pro Gly Glu Pro Arg Gly		
740	745	750
Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu		
755	760	765
Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val		
770	775	780
Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val		
785	790	795
Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val		
805	810	815
Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser		
820	825	830
Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met		
835	840	845
Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala		
850	855	860
Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro		
865	870	875
Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Met Thr Lys Lys Gln		
885	890	895
Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr		
900	905	910
Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr		
915	920	925
Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu		
930	935	940

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Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser
 945 950 955 960

Val Val His Glu Gly Leu His Asn His Thr Thr Lys Ser Phe Ser
 965 970 975

Arg Thr Pro Gly Lys
 980

<210> SEQ ID NO 526

<211> LENGTH: 753

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 526

Met Asp Ser Leu Ala Ser Leu Val Leu Cys Gly Val Ser Leu Leu Leu
 1 5 10 15

Ser Gly Thr Val Glu Gly Ala Met Asp Leu Ile Leu Ile Asn Ser Leu
 20 25 30

Pro Leu Val Ser Asp Ala Glu Thr Ser Leu Thr Cys Ile Ala Ser Gly
 35 40 45

Trp Arg Pro His Glu Pro Ile Thr Ile Gly Arg Asp Phe Glu Ala Leu
 50 55 60

Met Asn Gln His Gln Asp Pro Leu Glu Val Thr Gln Asp Val Thr Arg
 65 70 75 80

Glu Trp Ala Lys Lys Val Val Trp Lys Arg Glu Lys Ala Ser Lys Ile
 85 90 95

Asn Gly Ala Tyr Phe Cys Glu Gly Arg Val Arg Gly Glu Ala Ile Arg
 100 105 110

Ile Arg Thr Met Lys Met Arg Gln Ala Ser Phe Leu Pro Ala Thr
 115 120 125

Leu Thr Met Thr Val Asp Lys Gly Asp Asn Val Asn Ile Ser Phe Lys
 130 135 140

Lys Val Leu Ile Lys Glu Glu Asp Ala Val Ile Tyr Lys Asn Gly Ser
 145 150 155 160

Phe Ile His Ser Val Pro Arg His Glu Val Pro Asp Ile Leu Glu Val
 165 170 175

His Leu Pro His Ala Gln Pro Gln Asp Ala Gly Val Tyr Ser Ala Arg
 180 185 190

Tyr Ile Gly Gly Asn Leu Phe Thr Ser Ala Phe Thr Arg Leu Ile Val
 195 200 205

Arg Arg Cys Glu Ala Gln Lys Trp Gly Pro Glu Cys Asn His Leu Cys
 210 215 220

Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
 225 230 235 240

Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
 245 250 255

Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
 260 265 270

Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
 275 280 285

Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
 290 295 300

Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
 305 310 315 320

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Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
 325 330 335
 Gly Leu Gln Cys Glu Arg Glu Gly Ile Pro Arg Met Thr Pro Lys Ile
 340 345 350
 Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
 355 360 365
 Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
 370 375 380
 Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
 385 390 395 400
 Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
 405 410 415
 Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
 420 425 430
 Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
 435 440 445
 Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn
 450 455 460
 Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys
 465 470 475 480
 Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln
 485 490 495
 Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu
 500 505 510
 Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Glu Gly
 515 520 525
 His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro
 530 535 540
 Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn
 545 550 555 560
 Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val
 565 570 575
 Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys
 580 585 590
 Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg
 595 600 605
 Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu
 610 615 620
 Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro
 625 630 635 640
 Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val
 645 650 655
 Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile
 660 665 670
 Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys
 675 680 685
 Ile Lys Asn Ala Thr Ile Ile Gln Tyr Gln Leu Lys Gly Leu Glu Pro
 690 695 700
 Glu Thr Ala Tyr Gln Val Asp Ile Phe Ala Glu Asn Asn Ile Gly Ser
 705 710 715 720
 Ser Asn Pro Ala Phe Ser His Glu Leu Val Thr Leu Pro Glu Ser Gln
 725 730 735

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Ala Pro Ala Asp Leu Gly Gly Lys Ile Asp His His His His His
740 745 750

His

<210> SEQ_ID NO 527

<211> LENGTH: 498

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 527

Met Thr Val Phe Leu Ser Phe Ala Phe Leu Ala Ala Ile Leu Thr His
1 5 10 15

Ile Gly Cys Ser Asn Gln Arg Arg Ser Pro Glu Asn Ser Gly Arg Arg
20 25 30

Tyr Asn Arg Ile Gln His Gly Gln Cys Ala Tyr Thr Phe Ile Leu Pro
35 40 45

Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr
50 55 60

Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser
65 70 75 80

Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp
85 90 95

Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met
100 105 110

Ala Gln Ile Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu
115 120 125

Glu Ile Gly Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys
130 135 140

Leu Thr Asp Val Glu Thr Gln Val Leu Asn Gln Thr Ser Arg Leu Glu
145 150 155 160

Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln
165 170 175

Leu Leu Gln Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser
180 185 190

Leu Leu Glu His Lys Ile Leu Glu Met Glu Gly Lys His Lys Glu Glu
195 200 205

Leu Asp Thr Leu Lys Glu Glu Lys Glu Asn Leu Gln Gly Leu Val Thr
210 215 220

Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala
225 230 235 240

Thr Thr Asn Asn Ser Val Leu Gln Lys Gln Leu Glu Leu Met Asp
245 250 255

Thr Val His Asn Leu Val Asn Leu Cys Thr Lys Glu Gly Val Leu Leu
260 265 270

Lys Gly Gly Lys Arg Glu Glu Lys Pro Phe Arg Asp Cys Ala Asp
275 280 285

Val Tyr Gln Ala Gly Phe Asn Lys Ser Gly Ile Tyr Thr Ile Tyr Ile
290 295 300

Asn Asn Met Pro Glu Pro Lys Lys Val Phe Cys Asn Met Asp Val Asn
305 310 315 320

Gly Gly Gly Trp Thr Val Ile Gln His Arg Glu Asp Gly Ser Leu Asp
325 330 335

Phe Gln Arg Gly Trp Lys Glu Tyr Lys Met Gly Phe Gly Asn Pro Ser

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340 345 350

Gly Glu Tyr Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln
 355 360 365

Arg Gln Tyr Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg
 370 375 380

Ala Tyr Ser Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn
 385 390 395 400

Tyr Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser
 405 410 415

Ser Leu Ile Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn
 420 425 430

Asp Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp
 435 440 445

Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala
 450 455 460

Gly Gln Asn His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe Lys
 465 470 475 480

Gly Pro Ser Tyr Ser Leu Arg Ser Thr Thr Met Met Ile Arg Pro Leu
 485 490 495

Asp Phe

<210> SEQ ID NO 528

<211> LENGTH: 330

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 528

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
 65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
 100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
 145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 195 200 205

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Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> SEQ ID NO 529

<211> LENGTH: 327

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 529

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

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Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> SEQ ID NO 530
<211> LENGTH: 327
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: synthetic

<400> SEQUENCE: 530

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

-continued

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
 275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
 290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
 325

<210> SEQ ID NO 531
 <211> LENGTH: 88
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 531

Thr Ala Gly Lys Gln Ser Ser Leu Ile Leu His Gly Ala Asp Phe Ser
 1 5 10 15

Thr Lys Asp Ala Asp Asn Asp Asn Cys Met Cys Lys Cys Ala Leu Met
 20 25 30

Leu Thr Gly Gly Trp Trp Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn
 35 40 45

Gly Met Phe Tyr Thr Ala Gly Gln Asn His Gly Lys Leu Asn Gly Ile
 50 55 60

Lys Trp His Tyr Phe Lys Gly Pro Ser Tyr Ser Leu Arg Ser Thr Thr
 65 70 75 80

Met Met Ile Arg Pro Leu Asp Phe
 85

<210> SEQ ID NO 532
 <211> LENGTH: 7
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 532

Ser Leu Ser Leu Ser Pro Gly
 1 5

<210> SEQ ID NO 533
 <211> LENGTH: 8
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 533

Ser Leu Ser Leu Ser Pro Gly Lys
 1 5

<210> SEQ ID NO 534
 <211> LENGTH: 9
 <212> TYPE: PRT
 <213> ORGANISM: Homo sapiens

<400> SEQUENCE: 534

Glu Glu Gln Phe Asn Ser Thr Tyr Arg
 1 5

<210> SEQ ID NO 535
 <211> LENGTH: 13
 <212> TYPE: PRT

-continued

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 535

Thr	Lys	Pro	Arg	Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg
1				5				10				

What is claimed is:

1. A stable pharmaceutical formulation comprising:
 - (i) an antibody at a concentration of from 20 ± 3 mg/ml to 60 ± 9 mg/ml that binds specifically to human angiopoietin 2 (human Ang-2), wherein the antibody comprises a heavy chain variable domain (HCVD) having the amino acid sequence of SEQ ID NO:18 and a light chain variable domain (LCVD) having the amino acid sequence of SEQ ID NO:20;
 - (ii) histidine at a concentration of 10 ± 1.5 mM;
 - (iii) polysorbate 20 in an amount of $0.2\% \text{ w/v}\pm0.03\% \text{ w/v}$; and
 - (iv) sucrose in an amount of $10\% \text{ w/v}\pm1.5\% \text{ w/v}$, wherein the formulation has a pH of 6 ± 0.3 , and at least 92% of the antibody has native conformation when the formulation is kept at about 45°C . for up to about 28 days.
 2. The pharmaceutical formulation of claim 1, wherein
 - (a) over 96% of the antibodies have a molecular weight of $151 \text{ kDa}\pm1 \text{ kDa}$;
 - (b) at least 53% of the antibodies have an isoelectric point of about 8.13 ± 0.01 ; and
 - (c) from about 90% to about 92% of the antibodies are fucosylated.
 3. The pharmaceutical formulation of claim 1, wherein the antibody concentration is about $25 \text{ mg/mL}\pm0.375 \text{ mg/mL}$.
 4. The pharmaceutical formulation of claim 1, wherein the antibody concentration is about $50 \text{ mg/mL}\pm7.5 \text{ mg/mL}$.
 5. The pharmaceutical formulation of claim 1, wherein at least 93% of the antibody has native conformation after 28 days at 45°C .
 6. The pharmaceutical formulation of claim 1, wherein at least 32% of the antibody is the main charge variant of the antibody after 28 days at 45°C .
 7. The pharmaceutical formulation of claim 1, wherein at least 97% of the antibody has native conformation after 28 days at 25°C .
 8. The pharmaceutical formulation of claim 1, wherein at least 53% of the antibody is the main charge variant of the antibody after 28 days at 25°C .
 9. The pharmaceutical formulation of claim 1, wherein at least 96% of the antibody has native conformation after 28 days at 37°C .
 10. The pharmaceutical formulation of claim 1, wherein at least 45% of the antibody is the main charge variant of the antibody after 28 days at 37°C .
 11. The pharmaceutical formulation of claim 1, wherein at least 97% of the antibody has native conformation after six months at 5°C .
 12. The pharmaceutical formulation of claim 1, wherein at least 55% of the antibody is the main charge variant of the antibody after six months at 5°C .
 13. The pharmaceutical formulation of claim 1, wherein the percent relative potency of the antibody after six months at 5°C . is at least 100% of the potency of the antibody prior to storage.
- 10 14. The pharmaceutical formulation of claim 1, wherein at least 97% of the antibody has native conformation after six months at -80°C .
- 15 15. The pharmaceutical formulation of claim 1, wherein at least 55% of the antibody is the main charge variant of the antibody after six months at -80°C .
- 20 16. The pharmaceutical formulation of claim 1, wherein the percent relative potency of the antibody after six months at -80°C . is at least 85% of the potency of the antibody prior to storage.
- 25 17. The pharmaceutical formulation of claim 1, wherein at least 96% of the antibody has native conformation after six months at -30°C .
- 30 18. The pharmaceutical formulation of claim 1, wherein at least 55% of the antibody is the main charge variant of the antibody after six months at -30°C .
- 35 19. The pharmaceutical formulation of claim 1, wherein the percent relative potency of the antibody after six months at -30°C . is at least 84% of the potency of the antibody prior to storage.
- 40 20. The pharmaceutical formulation of claim 1, wherein at least 96% of the antibody has native conformation after six months at -20°C .
- 45 21. The pharmaceutical formulation of claim 1, wherein at least 55% of the antibody is the main charge variant of the antibody after six months at -20°C .
- 50 22. The pharmaceutical formulation of claim 1, wherein the percent relative potency of the antibody after six months at -20°C . is at least 90% of the potency of the antibody prior to storage.
- 55 23. A pharmaceutical formulation comprising (a) $25 \text{ mg/mL}\pm3.75 \text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10 \text{ mM}\pm1.5 \text{ mM}$ histidine, pH 6 ± 0.3 , (c) $0.2\% \text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\% \text{ w/v}\pm1.5\% \text{ sucrose}$, wherein:
 - (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20;
 - (b) over 96% of the antibodies have a molecular weight of $151 \text{ kDa}\pm1 \text{ kDa}$;
 - (c) at least 53% of the antibodies have an isoelectric point of about 8.13 ± 0.01 ; and
 - (d) from about 90% to about 92% of the antibodies are fucosylated.
- 60 24. The pharmaceutical formulation of claim 23 consisting of (a) $25 \text{ mg/mL}\pm3.75 \text{ mg/mL}$ of the antibody, (b) $10 \text{ mM}\pm1.5 \text{ mM}$ histidine, pH 6 ± 0.3 , (c) $0.2\% \text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\% \text{ w/v}\pm1.5\% \text{ sucrose}$, in water.
- 65 25. A pharmaceutical formulation comprising (a) $50 \text{ mg/mL}\pm7.5 \text{ mg/mL}$ of an anti-Ang-2 antibody, (b) $10 \text{ mM}\pm1.5 \text{ mM}$ histidine, pH 6 ± 0.3 , (c) $0.2\% \text{ w/v}\pm0.03\%$ polysorbate 20, and (d) $10\% \text{ w/v}\pm1.5\% \text{ sucrose}$, wherein:
 - (a) the antibody comprises an HCVD of SEQ ID NO: 18 and an LCVD of SEQ ID NO: 20;
 - (b) over 96% of the antibodies have a molecular weight of $151 \text{ kDa}\pm1 \text{ kDa}$;
 - (c) at least 53% of the antibodies have an isoelectric point of about 8.13 ± 0.01 ; and

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(d) from about 90% to about 92% of the antibodies are fucosylated.

26. The pharmaceutical formulation of claim **25** consisting of (a) 50 mg/mL \pm 7.5 mg/mL of the antibody, (b) 10 mM \pm 1.5 mM histidine, pH 6 \pm 0.3, (c) 0.2% w/v \pm 0.03% polysorbate 20, and (d) 10% w/v \pm 1.5% sucrose, in water. 5

27. A pharmaceutical composition comprising the formulation of claim **1**, wherein said composition is contained in a container.

28. The pharmaceutical composition of claim **27**, wherein the container is a vial. 10

29. The pharmaceutical composition of claim **28**, wherein the vial is glass.

30. The pharmaceutical composition of claim **27**, wherein the container is an intravenous drip bag. 15

31. The pharmaceutical composition of claim **30**, wherein the bag is made of polyvinyl chloride.

32. The pharmaceutical composition of claim **30**, wherein the bag is made of polyolefin.

33. A kit comprising a pharmaceutical composition of claim **27**, and instructions. 20

34. The kit of claim **33**, wherein the container is a glass vial fitted with a fluorocarbon coated rubber stopper.

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